<u>SUBSTITUTE SPECIFICATION</u>

5   ~~THE TRADITIONAL CHINESE MEDICINE PREPARATION FOR TREATMENT OF TUMOR AND METHOD OF MAKING AND USING SAME~~<u>The Traditional Chinese Medicine Preparation For Treatment Of Tumor And Method Of Making And Using Same</u>

Field of the Invention

10   This invention involves in the fields of Traditional Chinese Medicine, in particularly, involves in a kind of Traditional Chinese Medicine preparation, its preparative methods and applications in the procedure of preparing anti-tumor drugs.

Background of the Invention

15   Cancer is one of the most serious diseases which severely threaten our ~~healths~~ health. According to the statistical materials, at present there are more than 18 million cancer patients all over the world. It is predicted that the cancer incidence will increase by 50% than that of present level, there will be 15 million new cancer cases by the year 2020 when the average onset age of cancer patient will be about 40, while now it ranges from 50 to 60, in certain cities, onset age of gastric cancer is 35, it is quite frightening.

20   In the field of cancer therapy, in addition to traditional therapy methods such as surgical excision, chemotherapy and radiotherapy, scientists and medical workers are now trying hard to explore and find new means and methods that can radically cure cancer-, for example, cryotherapy under 180 degree below zero, heat therapy using microwave solidification; starve tumor treatment, that is to say, blocking the blood vessels and cutting the nutrition supply of tumor; adopting biotechnology, necrosis factors, gene therapy and many

25   other methods to treat cancers, but considering the present technology level and medical conditions at home and abroad, all of the new anti –tumor methods mentioned above still can't reach scientific conclusions because of lacking prospective study, while hoping to find new drugs which can treat cancers from Traditional Chinese Medicines, which becomes the focus of international anti-cancer fields.

Traditional Chinese Medicine and Traditional Chinese Medicine theories are one of the most precious

30   cultural heritages, they are basic protections of ancient Chinese living and breeding, at the same time, those abounding experiences and theories are formed in the courses of fighting with diseases which still play important roles in modern civilized society.

The anti-cancer effects of Traditional Chinese Medicine have been approved by Chinese people and western countries, however anti- cancer Traditional Chinese Medicine used in the whole clinical medication only

35   account for 3—5%, meanwhile, there is no anti-cancer Traditional Chinese Medicine used for the treatment

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of gastric cancer.

The idea of developing and inventing a kind of safe, effective and controllable anti-cancer. Traditional Chinese Medicine preparation (not prescription), which can be widely used in clinical work is the basic guiding throught thought of this invention.

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Summary of the Invention

This invention is based on the Traditional Chinese Medicine theory on cancer: "Cancer is caused by stagnation of vital energy and blood stasis which further give rise to lump and tumor accumulation and should be treated with the strategies of promoting blood flow and removing blood stasis; eliminating toxic
10   material and SanJie", combined with modern medicine theories, using modern technology, carefully screening the herbs in order to meet three purposes: to supply a kind of anti-tumor traditional Chinese medicine preparation; to supply the preparative method; to supply its application in the preparation of anti-tumor drugs.

The purpose of this invention is realized as follows: A kind of anti-tumor, traditional Chinese medicine
15   preparation, its' feature is that this preparation is composed of following parts by weight of materials: 1 parts by weight of hydnocarpus, 0.8-1.4 parts by weight of cochinchina momordica seed, 0.5-1.1 parts by weight of pangolin scales, 0.8-1.3 parts by weight of rhubarb, 1-1.5 parts by weight of licorice root.

Ofof which, the herb "hydnocarpus" is adopted which can enter liver spleen meridian, its fatty acid glycerolipid that has the functions of eliminating wind, depriving the evil wetness, expelling toxin, relieving
20   sputum and accumulating water serves as principal drug.

The herb "cochinchina momordica seed" is adopted which can enter spleen stomach meridian, its momordic acid that has the functions of detumescence, expelling toxin and promoting tissue regeneration serves as ministerial drug.

The herb "pangolin scales" is adopted which can enter liver stomach meridian, its pangolin scales alkali that
25   has the functions of detumescence, relieving ache, removing the wind, activating collaterals, treating crewels and ulcer and fighting papillary cancer cells serves as adjunctive drug.

The herb "rhubarb" is adopted which can enter stomach intestine meridian, its emodin and rhrum tannic acids that have the functions of removing pyretic toxicity, breaking dyspeptic disease and improving microcirculation serves as adjunctive drug.
30   The herb "licorice root" is adopted which can enter spleen stomach meridian, its enoxolone that has the functions of anti-cancer, neutralizing poison and coordinating the drug actions of a prescription serves as messenger drug. In this invention, the optimum dosage of each crude herb is 1 parts by weigh.

Preparative methods of anti-tumor Traditional Chinese medicine preparation in this invention include the following steps:
35   1）Weighing each crude herb, grinding to middle size particles,

    2）Adding 62% ethyl alocohol alcohol in a w/v of 1:2.5~1:3.5 with crude herbs and soaking thoroughly,

    3）Heating and recirculating fully,

    4）Filtrating, filter liquor acquired is the active ingredient solution of the Traditional Chinese Medicine preparation mentioned in this invention.

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In this invention, to the residues and gruffs gotten in step 4, adding 62% ethyl ~~alocohol~~ alcohol in a w/v of 1:0.8~1:1.5, heating again and recirculating thoroughly, filtrating, ~~;~~filter liquor ~~aquired~~ acquired is combined with filter liquor ~~aquired~~ acquired in the former steps, the combined liquid also is the active ingredient solution of the Traditional Chinese Medicine preparation mentioned in this invention.

5 The optimum w/v in this method is 1:1.

Heating and recirculating time mentioned in the method is 0.5-1 hour generally.

Adjusting active ingredient solution with ethyl ~~alocohol~~ alcohol and water, making ethyl ~~alocohol~~ alcohol volume percentage to be 6.0-8.0%, adjusting pH to be 4.0-5.0, then the composition of the Traditional Chinese Medicine preparation mentioned in this invention is completely made.

10 The best relative density of this composition of the Traditional Chinese Medicine preparation is 1.02-1.08.

Or drying the active ingredient solution of the Traditional Chinese Medicine preparation mentioned above and making it into granula, filling granula into blank capsules, then the capsule of the Traditional Chinese Medicine preparation mentioned in this invention is completely made.

Alternatively, drying the active ingredient solution of the Traditional Chinese Medicine preparation

15 mentioned above and compressing into round lamellar shape, the tablets of the Traditional Chinese Medicine preparation in this invention is ~~eonpletely~~ completely made.

Hydnocarpus and cochinchina momordica seed are two poisonous herbs in the composition, the standard dosage and maximum dosage is 15g each day, dosage more than 15g will cause lowering blood pressure, short of breath, accelerating of heart beat, vomit, anepithymia, insomnia, haemolytic anemia, nephritis

20 hyperproteinuria and erythrocyturia and other adverse reactions, on the contrary, if the dosage is less than 15 g each day, the anti-cancer effect will be poor or even ineffective ~~completetly~~ completely.

The Traditional Chinese Medicine preparation in this invention has many advantages: the herb is well organized, compatibility is reasonable, principal, adjuvant, auxiliary and conductant ingredients are highlighted, dosage is accurate, safe and effective, any herb can not be added or reduced, increasing dosage

25 will enhance toxicity, decreasing dosage will result in poor anti-cancer effects It not only has the functions of eliminating pathogen via promoting blood flow, improving microcirculation and counteracting toxic substance, but also has the functions of strengthening body resistance via rising WBC and promoting tissue regeneration. ~~this~~ This highly coincides with the Traditional Chinese Medicine theory of cancer therapy, that is, treating the malignant with poisonous agents, eliminating pathogen to support vital qi, it also

30 coincides with modern medicine theory of enhancing phagocytosis function of macrophage, improving the immune system of the patients and inhibiting and killing cancer cells.

The invention was substantiated by animal experiments and clinic trails, and was proved to be safe, effective and controllable.

The invention surmount other drugs which has simple function such as strengthening body resistance ,

35 synergism or attenuation, it possess four ~~founetions~~ functions (eliminating pathogen, strengthening body resistance, synergism , attenuation) at the same time.

The invention can solely be used as anti-cancer drug, it also can be combined to use with chemotherapy

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drugs, when combined to use, the Traditional Chinese Medicine preparation of this invention can not only greatly reduce severe adverse reactions of chemotherapy, but also greatly improve its short term therapeutic efficacy and prostecdtive efficacy (outweighing chemotherapy), thus could enhance anti-cancer effects.

The Traditional Chinese Medicine preparation of this invention can be widely used for the treatment of tumor such as digestive tract tumor including gastric cancer, intestines cancer, liver cancer, esophageal cancer, other cancers like lung cancer, uterine cervix cancer, breast cancer, skin cancer etc, particularly, gastric cancer and liver cancer patients have good therapeutic response to the invention.

Detailed Description of the Invention

Example 1   Preparation of Traditional Chinese Medicine composition of the invention.

150g of hydnocarpus, 150g of cochinchina momordica seed, 150g of pangolin scales, 150g of rhubarb and 150g of licorice root. Grinding all above five herbs into middle size granula, adding 2500 ml of 62% ethyl alcohol , soaking for 12 hours, heating and recirculating for 1 hour, filtrating, adding 800 ml **of   62%** ethyl alcohol into gruffs and heating again, recirculating for 1 hour, filtrating and combining all of the filter liquors, decompressing and condensing to 950 ml, adjusting to 1000 ml with ethyl alcohol and water, making the volume of ethyl alcohol to be 6.0~8.0%, adjusting pH to be 4.0~5.5, regulating relative density to be 1.05, mixing evenly, standing still at 6-10℃ for 12 hours, centrifugating and extracting supernatant, bottling and thus getting the composition.

Example 2   Preparation of Traditional Chinese Medicine composition of the invention.

150g of hydnocarpus, 240g of cochinchina momordica seed, 120g of pangolin scales, 120g of rhubarb and 225g of licorice root.   Grinding all above five herbs into middle size granula, adding 2600 ml of 62% ethyl alcohol, soaking for 18 hours, heating and recirculating for 1 hour, filtrating, adding 900 ml of 62% ethyl alcohol into gruffs and heating again, recirculating for 1 hour, filtrating and combining all of the filter liquors, decompressing and condensing to 950 ml, adjusting to 1000 ml with ethyl alcohol and water, making the volume of ethyl alcohol to be 6.0~8.0%, adjusting pH to be 4.0~5.5, regulating relative density to be1.02, mixing evenly, standing still at 6-10℃ for 12 hours, centrifugating and extracting supernatant, bottling and thus getting the composition.

Example 3   Preparation of Traditional Chinese Medicine composition of the invention.

80g of hydnocarpus, 75g of cochinchina momordica seed, 50g of pangolin scales, 75g of rhubarb and 100g of licorice root.   Grinding all above five herbs into middle size granula, adding 950 ml of 62% ethyl alcohol, soaking for 12 hours, heating and recirculating for 1 hour, filtrating, adding 320 ml of 62% ethyl alcohol into gruffs and heating again, recirculating for 1 hour, filtrating and combining all of the filter liquors, decompressing and condensing to 950 ml, adjusting to 1000 ml with ethyl alcohol and water, making the volume of ethyl alcohol to be 6.0~8.0%, adjusting pH to be 4.0~5.5, regulating relative density to be 1.06, mixing evenly, standing still at 6-10℃ for 12 hours, centrifugating and extracting supernatant, bottling and thus getting the composition.

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Example 4   Preparation of Traditional Chinese Medicine composition of the invention.

120g of hydnocarpus, 140g of cochinchina momordica seed, 100g of pangolin scales, 150g of rhubarb and 180g of licorice root.   Grinding all above five herbs into middle size granula, adding 2000 ml of 62% ethyl alcohol, soaking for 12 hours, heating and recirculating for 1 hour, filtrating, adding 700 ml of 62% ethyl

5   alcohol into gruffs and heating again, recirculating for 1 hour, filtrating and combining all of the filter liquors, decompressing and condensing to 950 ml, adjusting to 1000 ml with ethyl alcohol and water, making the volume of ethyl alcohol to be 6.0~8.0%, adjusting pH to be4.0~5.5, regulating relative density to be 1.08, mixing evenly, standing still at 6-10℃ for 12 hours, centrifugating and extracting supernatant, bottling and thus getting the composition.

10   Example 5   Preparation of Traditional Chinese Medicine capsules of the invention.

180g of hydnocarpus, 180g of cochinchina momordica seed, 90g of pangolin scales, 150g of rhubarb and 250g of licorice root. Grinding all above five herbs into middle size granula, adding 2500 ml of 62% ethyl alcohol , soaking for 24 hours, heating and recirculating for 1 hour, filtrating, adding 1000 ml of 62% ethyl alcohol into gruffs and heating again, recirculating for 1 hour, filtrating and combining all of the filter

15   liquors, drying and making into uniform granula and filling them into vacant capsules, thus forming hard capsules.

Example 6   Preparation of Traditional Chinese Medicine tablets of the invention.

100g of hydnocarpus, 80g of cochinchina momordica seed, 110g of pangolin scales, 130g of rhubarb and 150g of licorice root.   Grinding all above five herbs into middle size granula, adding 1500 ml of 62% ethyl

20   alcohol , soaking for 18 hours, heating and recirculating for 0.5 hour, filtrating, adding 750 ml of 62% ethyl alcohol into gruffs and heating again, recirculating for 1 hour, filtrating and combining all of the filter liquors, drying and compressing them into ground lamellar shape, thus getting the tablets.

Test example 1: Pharmacodynamics research of the Traditional Chinese Medicine preparation of this invention.

25   I Tested Drugs

1. Preparation labeled dosage: 1 ml containing 0.55g of crude drug

2. Solvent: 0.5％CMC－Na

3. Preparative methods: stock solution was diluted to demanding concentration with 0.5％CMC－Na, giving 0.5 ml of drug to each mouse each time.

30   II Animals

1. Name, source, Strain: BALB/c mice or F1 (ICR×BALB/c) ,mice and Kunming mice, animal group of our institute. C57BL/6 mice and nu /BALB/c mice were purchased from Shanghai laboratory animal center.

2. Weight: 19±1g, 6-8 weeks old.

3. Sex: male or female, using the same sex for each study.

4. Animal breeding and experiment conditions: Kunming mice, C57BL/6 mice and F1 mice were kept in Clean Animal Laboratory,nu/BALB/c mice were kept in lamina flow framework and raised according to SPF condition, administration was given in the lamina flow framework.

5   5. The number of animal of each group: tested group, three dosage.   Positive group, and blank group. 6 nu/BALB/c mice each group, 10 Kunming mice, 10 C57BL/6 mice and 10 F1 mice each group.

III Test Method Choice

According to 《Guideline for Traditional Chinese Medicine Research》, performing study on eliminating pathogen to strengthen body resistance, attenuation and synergism function

10   Considering that it is a compound preparation, it should adopt the whole animal test.

IV Dosage

po(take orally), 25.0, 12.5 and 6.25ml/kg or 75, 37.5 and 18.75ml/M2 for high dosage, middle dosage, low dosage respectively.

ip (intraperitoneal injection) 10.0, 5.0 and 2.5ml/kg for high dosage, middle dosage, low dosage

15 respectively.

V Administration manner

po×10qd and ip×10qd for ~~studing~~ studying on eliminating pathogen, strengthening body resistance, attenuation and synergism function, of which, po is the administration manner for clinical medication; Studying on strengthening body resistance function only use po path, implementing ~~12.5, 6.25,~~

20   ~~3.125ml/kg~~ 12.5, 6.25, 3.125ml/kg po×10 regimen

VI Controls

Blank: solvent 0.5％CMC－Na.

Positive drug control: Considering that there is no suitable corresponding positive control, it should choose cyclophosphamide as positive control, in order to substantiate authenticity of each test.

25 VII. Test Main Steps and Results

1. Eliminating pathogen function study

Test on xenogeneic graft mice models of human gastric cancer cell line MKN and human liver cancer cell line QGY: Taking related cancer cells, preparing to homogenate containing $1-2\times10^7$ tumor cells/ml, ~~chosing~~ choosing corresponding recipient mice, armpit hypodermic inoculation 0.2 ml or pedis hypodermic

30 inoculation 0.05 ml of tumor cell suspension, randomization, giving therapy according to the administration regimen next day, dissecting each test group tumor after 2 weeks and comparing with control group, calculating inhibition ratio, all the procedure should be performed strictly under sterilized condition, results are shown in table 1-4

Inhibition test on animal-transplanted tumor such as mice colon carcinoma C26 and Lewis lung carcinoma,

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methods are the same as above, and the results are shown in table 5-10.

note: "***"represents P<0.01; "**"represents P<0.05; "*"represents P<0.1。

Table 1. Therapeutic effects test of invented composition on xenogeneic graft mice models of human gastric cancer cell line MKN via po

sample group	dosage ml/kg ml/M²	administration regimen	mice number beginning end	weight beginning end	tumor weight $\bar{x}\pm SD$	inhibition ratio %
invented ~~composition~~ ~~25~~ ~~75~~ ~~po×10qd~~ ~~6~~ ~~6~~ ~~17.6~~composition 25 75 po×10qd 6 6 17.6 17.1 0.317±0.12 77.83***						
invented ~~composition~~ ~~12.5~~ ~~37.5~~ ~~po×10qd~~composition 12.5 37.5 po×10qd 6 6 17.7 17.7 0.717±0.12 49.86***						
invented composition 6.25 18.75 po×10qd 6 6 17.8 17.4 1.12±0.23 21.68						
positive control cyclophosphamide 30mg/kg ip×7qd 6 6 17.7 16.6 0.17±0.15 88.11***						
negative control solvent po×10qd 12 12 17.5 19.9 1.43±0.24						

~~table2~~Table 2. Therapeutic effects test of invented composition on xenogeneic graft mice models of human gastric cancer cell line MKN via peritoneal injection

sample group	dosage ml/kg ml/M²	administration regimen	mice number beginning end	weight beginning end	tumor weight ~~x̄±SD~~$\bar{x}\pm SD$	inhibition ratio %
invented composition	10 30	ip×10qd	6 6	18.3 17.7	0.25±0.10	80.47***
invented composition	5 15	ip×10qd	6 6	18.5 18.4	0.53±0.12	58.59***
invented composition	2.5 7.5	ip×10qd	6 6	18.2 18.6	0.90±0.26	26.69
positive control cyclophosphamide	30mg/kg	ip×7qd	6 6	18.0 17.9	0.14±0.05	89.06***
negative control	solvent	ip×10qd	12 12	18.1 20.1	1.28±0.26	

~~table3~~Table 3. Therapeutic effects test of invented composition on xenogeneic graft mice models of human liver cancer cell line QGY via po

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sample group	dosage ml/kg	ml/M²	administration regimen	mice number beginning	end	weight beginning	end	tumor weight $\bar{x}\pm SD$	inhibition ratio %
invented composition	25	75	po×10qd	6	6	17.4	17.9	1.13±0.22	49.33***
invented composition	12.5	37.5	po×10qd	6	6	17.7	18.0	1.48±0.30	33.63**
invented composition	6.25	18.75	po×10qd	6	6	17.5	17.9	1.65±0.20	26.00
positive control	30mg/kg								
cyclophosphamide			ip×7qd	6	6	17.6	17.0	0.25±0.14	88.79***
negative control	solvent		po×10qd	12	12	17.5	19.4	2.23±0.31	

~~table4~~Table 4. Therapeutic effects test of invented composition on xenogeneic graft mice models of human liver cancer cell line QGY via peritoneal injection

sample group	dosage ml/kg	ml/M²	administration regimen	mice number beginning	end	weight beginning	end	tumor weight $\bar{x}\pm SD$	inhibition ratio %
invented composition	10	30	ip×10qd	6	6	17.3	18.1	1.03±0.29	48.76***
invented composition	5	15	ip×10qd	6	6	17.2	18.7	1.37±0.23	31.84**
invented composition	2.5	7.5	ip×10qd	6	6	16.8	18.4	1.60±0.24	20.40
positive control	30mg/kg								
cyclophosphamide			ip×7qd	6	6	17.0	17.6	0.22±0.08	89.05***
negative control	solvent		ip×10qd	12	12	17.3	19.5	2.01±0.33	

~~table5~~Table 5. Therapeutic effects test of invented composition on mice C26 colon solid tumor via po

sample group	dosage ml/kg	ml/M²	administration regimen	mice number beginning	end	weight beginning	end	tumor weight $\bar{x}\pm SD$	inhibition ratio %
invented composition	25	75	po×10qd	10	10	21.2	24.7	1.38±0.22	43.67***
invented composition	12.5	37.5	po×10qd	10	9	21.4	25.2	1.71±0.36	30.2**
invented composition	6.25	18.75	po×10qd	10	10	21.3	25.7	2.24±0.25	8.6

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sample group	dosage ml/kg	ml/M²	administration regimen	mice number beginning	end	weight beginning	end	tumor weight $\bar{x}\pm SD$	inhibition ratio %
positive control cyclophosphamide	30mg/kg		ip×7qd	10	10	21.3	22.6	0.22±0.06	91.02***
negative control	solvent		po×10qd	20	20	21.3	26.2	2.45±0.57	

table6Table 6. Therapeutic effects test of invented composition on mice C-26 colon solid tumor via peritoneal injection

sample group	dosage ml/kg	ml/M²	administration regimen	mice number beginning	end	weight beginning	end	tumor weight $\bar{x}\pm SD$	inhibition ratio %
invented composition	10	30	ip×10qd	10	10	20.1	23.1	1.36±0.20	49.91***
invented composition	5	15	ip×10qd	10	10	20.3	23.9	1.70±0.37	37.98**
invented composition	2.5	7.5	ip×10qd	10	10	20.4	23.4	2.12±0.47	21.92
positive control cyclophosphamide	30mg/kg		ip×7qd	10	10	20.2	21.0	0.22±0.06	91.90***
negative control	solvent		ip×10qd	20	20	20.4	24.8	2.75±0.45	

table7Table 7. Therapeutic effects test of invented composition on mice C-26 colon carcinoma (pedis inoculation) via po

sample group	dosage ml/kg	ml/M²	administration regimen	mice number beginning	end	weight beginning	end	tumor weight $\bar{x}\pm SD$	inhibition ratio %
invented composition	25	75	po×10qd	10	10	19.3	21.0	0.41±0.07	54.95***
invented composition	12.5	37.5	po×10qd	10	10	19.2	21.7	0.55±0.11	39.56***
invented composition	6.25	18.75	po×10qd	10	10	19.1	22.3	0.70±0.15	23.08
positive control cyclophosphamide	30mg/kg		ip×7qd	10	10	19.1	20.4	0.19±0.06	79.12***
negative control	solvent		po×10qd	20	20	19.3	24.9	0.91±0.18	

table8Table 8. Therapeutic effects test of invented composition on mice C-26 colon carcinoma (pedis

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inoculation) via peritoneal injection

sample group	dosage ml/kg	ml/M²	administration regimen	mice number beginning	end	weight beginning	end	tumor weight $\bar{x}\pm SD$	inhibition ratio %
invented composition	10	30	ip×10qd	10	10	19.0	21.7	0.42±0.06	56.48***
invented composition	5	15	ip×10qd	10	10	18.9	21.4	0.58±0.11	39.90***
invented composition	2.5	7.5	ip×10qd	10	10	18.7	22.3	0.75±0.20	22.28
positive control	30mg/kg								
cyclophosphamide			ip×7qd	10	10	18.7	20.0	0.18±0.06	81.35***
negative control	solvent		ip×10qd	20	20	18.8	23.1	0.965±0.18	

table9Table 9. Therapeutic effects test of invented composition on mice Lewis lung solid tumor via po

sample group	dosage ml/kg	ml/M²	administration regimen	mice number beginning	end	weight beginning	end	tumor weight $\bar{x}\pm SD$	inhibition ratio %
invented composition	25	75	po×10qd	10	9	18.4	19.4	1.51±0.90	40.08***
invented composition	12.5	37.5	po×10qd	10	10	18.7	20.0	1.72±0.38	31.75**
invented composition	6.25	18.75	po×10qd	10	10	18.5	20.8	1.92±0.27	23.81
positive control	30mg/kg								
cyclophosphamide			ip×7qd	10	10	18.8	19.3	0.29±0.07	88.49***
negative control	solvent		po×10qd	20	20	18.5	22.0	2.52±0.61	

table10Table 10. Therapeutic effects test of invented composition on mice Lewis lung solid tumor via peritoneal injection

sample group	dosage ml/kg	ml/M²	administration regimen	mice number beginning	end	weight beginning	end	tumor weight $\bar{x}\pm SD$	inhibition ratio %
invented composition	10	30	ip×10qd	10	10	18.3	19.9	1.18±0.27	44.86***
invented composition	5	15	ip×10qd	10	10	18.3	20.4	1.41±0.43	34.11**

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invented composition 2. 5 7. 5	ip×10qd	10	10	18. 5	20. 7	1. 57±0. 53	26. 64
positive control 30mg/kg							
cyclophosphamide	ip×7qd	10	10	18. 3	19. 4	0. 25±0. 07	88. 32***
negative control solvent	ip×10qd	20	20	18. 6	22. 7	2. 14±0. 27	

Through vivo anti—tumor therapeutic effect study, it demonstrates that the Traditional Chinese Medicine composition of the invention has a relatively high tumor inhibition rate when used at a high dosage of 25ml/kg po×10 and 10ml/kg ip×10 on xenogeneic graft mice models of human gastric cancer cell line MKN, the average inhibition rate is 79.75% and 81.54% respectively, which is 2.7 times higher than the level of government regulation (30%), middle dosage 12.5ml/kgpo×-10 and 5ml/kg ip×10 also have a moderate tumor inhibition rate, the average inhibition rate is 53.89% and 58.80% respectively.   For other animal-transplanted tumor such as colon carcinoma C-26 and Lewis lung carcinoma, xenogeneic graft mice models of human liver cancer cell line QGY, high dosage of invented composition via po or ip both have a moderate anti-tumor effect. Of which, effect of peritoneal injection is better than that of po. Main pharmacodynamics study shows that the invented Traditional Chinese Medicine composition has obvious eliminating pathogen functions.

2.Strengthening body resistance function study

1) Influence of invented Traditional Chinese Medicine composition on phagocytosis function of macrophages exists in the Kunming mice abdominal cavities: Randomly dividing male Kunming mice into several groups, 10 mice each group. Giving composition via po for consecutive 10 days, once each day. Peritoneal injection 1.5 ml of 0.5% aminopeptodrate for each group of mouse after the last administration of composition, then 24 hours later, peritoneal injection 0.2 ml of chicken red blood cells suspension at a concentration of $1×10^6$/ml,40 minutes later, washing and collecting mice peritoneal fluid with physiologic saline, centrifugated, collecting cell sediments and making into smear, mehanol fixation, Giemsa staining, mounting. Counting 100 macrophages using immersion objective, Counting the number of macrophage that phagocytized chicken red blood cells and counting total number of phagocytized chicken red blood cells. Calculating phagocytosis percentage and phagocytosis index according to following formula, and the results are shown in table 11.
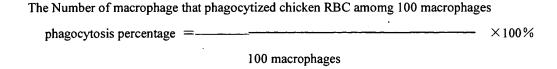
$$\text{phagocytosis percentage} = \frac{\text{The Number of macrophage that phagocytized chicken RBC amomg 100 macrophages}}{100 \text{ macrophages}} \times 100\%$$

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$$\text{phagocytosis index} = \frac{\text{total number of phagocytized chicken RBC among 100 macrophages}}{100 \text{ macrophage}}$$

5   Table 11 Influence of invented composition on phagocytosis function of macrophages exists in the Kunming mice abdominal cavities

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sample group	dosage ml/kg	administration regimen	mice number	phagocytosis percentage $\bar{x} \pm SD\%$	phagocytosis index
composition	12.5	po×10qd	10	38.4±6.48**	0.77±0.06***
control	solvent	po×10qd	10	26.7±7.32	0.53±0.08
composition	12.5	po×10qd	10	39.6±5.10**	0.58±0.05***
control	solvent	po×10qd	10	29.2±4.6	0.33±0.07
15 composition	12.5	po×10qd	10	39.6±5.10**	0.58±0.05***
control	solvent	po×10qd	10	29.2±4.6	0.33±0.07

2) Influence of invented Traditional Chinese Medicine composition on NK cell activity of the Lewis lung

20   carcinoma bearing mice: hypodermic inoculating 1×106 Lewis lung carcinoma cell suspensions on C57BL/6 right pedis, regimen 12.5、6.25 and 3.125ml/kg po×7qd was implemented on the following day with invented composition. after-After all administration was finished, killing all the mice, taking out spleen and collecting spleen cells, making into effector cells at a concentration of $1×10^7$/ml. using cultured Yac-1 cells as target cells, concentration is $1×10^6$/ml, taking out these two cells 100ul respectively and adding into 96 well plate,

25   adding $1.75×104$Bq/well of ^{3}H-TdR and culturing for 24 hours, collecting cells, assaying cpm value of each well with Liquid Scintillation Counters and calculating the obvious difference between test groups and control groups(shown in tableTable 12)

Table 12. Influence of invented composition on NK cell activity of cancer bearing mice

30

sample group	dosage ml/kg	administration regimen	CPM value $\bar{x} \pm SD$
invented composition	12.5	po×10qd	4213±728 **

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invented composition	6. 25	po×10qd	3746±835 **
invented composition	3. 125	po×10qd	4306±663 **
control		po×10qd	5996±908

invented composition	12. 5	po×10qd	3628±551 **
invented composition	6. 25	po×10qd	3150±908 **
invented composition	3. 125	po×10qd	3726±1141 **
control		po×10qd	4938±871

5

10   The invented Traditional Chinese Medicine composition can obviously enhance the phagocytosis functions of macrophages in the mice abdominal cavities; at the same time, it can enhance NK cell activity of Lewis lung carcinoma bearing mice to some extent.

3.Synergistic effect study

15   Hypodermic inoculating S180 sarcomas homogenate on Kunming mice armpit, dividing mice into different groups next day, solely used group: the invented Traditional Chinese Medicine composition, 25.0、12.5、6.25ml/kg po×10; combinely combinedly used group: 25.0、12.5、6.25ml/kg po×10 plus 15mg/kg cyclophosphamide ip×7, 12days after inoculation, dissecting tumors, measuring average tumor weight of each group and calculating standard deviation, comparing test group with control group and calculating

20   tumor inhibition rate, and the results demonstrate that high dosage of invented Traditional Chinese Medicine composition, combined with low dosage of cyclophosphamide, produces certain synergism effects on the treatment of S180 sarcomas(shown in table13 Table 13).

Table 13. Therapeutic effects of the invented composition combined with cyclophosphamide on S_{180}

25

sample group	dosage ml/kg	administration regimen	tumor weight (g) $\bar{x}\pm SD$	inhibition rate %
invented composition	25.0	po×10	1.19±0.36	61.73***
invented composition	12.5	po×10	1.69±0.29	45.66***
invented composition	6.25	po×10	2.15±0.27	30.87***
invented composition	25.0	po×10	0.88±0.31	71.70***
CTX	15.0mg/kg	ip×7		

30

13

invented composition 12.5		po×10	1.55±0.40	50.16***
CTX	15.0mg/kg	ip×7		
invented composition 6.25		po×10	1.84±0.24	40.84***
CTX	15.0mg/kg	ip×7		
CTX	15.0mg/kg	ip×7	1.71±0.25	45.02***
CTX	30.0mg/kg	ip×7	0.49±0.12	84.24***
control	solvent	po×10	3.10±0.46	
control	solvent	po×10		

4. Attenuation function study

Cyclophosphamide 100mg/kg ip×2 was given to F1 mice, then randomly divided into three different groups, treated with 25.0、12.5、6.25ml/kg po×10qd of the invented Traditional Chinese Medicine composition, counting white blood cells every four days, getting average number and standard deviation, setting the WBC number of 0 day as 100%, calculating WBC percentage of each timepoint, it shows that the invented composition has no significant functions of rising WBC, at the same time, it also has no effects of enhancing WBC inhibition (shown in table14Table 14).

Table 14. Attenuation function of the invented composition on WBC inhibition caused by cyclophosphamide

sample group	dosage ml/kg	administration regimen	WBC percentage					
			0d	3d	6d	9d	12d	15d
invented composition	25.0	po×10qd	100	39.4	45.6	57.2	68.1	98.9
invented composition	12.5	po×10qd	100	36.7	42.1	54.8	64.0	99.5
invented composition	6.25	po×10qd	100	35.9	44.2	51.4	62.1	103.3
solvent		po×10qd	100	33.1	42.8	48.3	59.4	92.6

Test example 2 In in vitro **anti-tumor cell proliferation test of the invented Traditional Chinese Medicine composition**

Ⅰ. Tested drugs

14

1. Content potency: 1ml containing 0.55g of crude drug.

2. Preparative methods: dissolved in the culture medium containing fetal bovine serum, preparing each time when used.

II. Cell strains

5   Human lung cancer cell line (Al).

Human cervical carcinoma cell line (Hela).

Source: cell bank of Shanghai Institute of Cell Biology.

III. Main experiment steps

1. Seeding tumor cells into culture bottle, 130 thousand unit each bottle.

10   2. Dividing into different dosage groups

3. Adding culture medium containing specified dosage of tested composition and control drug respectively.

4. Counting the number of cells in different group within in defined time.

IV. Specification of index and time

15   Observing inhibition rate of different dosage composition on tumor cells and drug concentration on inhibiting concentration (IC50, observing time is 4 days.

V. Dosage setting

Five dosage, they are 0.55, 2.75, 5.5, 13.75, 27.5mg/ml respectively.

VI. Administration manner

20   Composition is added into culture medium and used to culture cells directly.

VII. Controls

chosing canelim capsule as control, ground into powder and steriled, dissolved into medium and centrifugated, divided into 0.3, 1.5, 3, 7.5, 15mg/ml five dosage, administration manner is the same as above.

VIII. Results:

25   The invented composition can inhibit human tumor cells Hela and Al proliferation in a manner of dosage dependence, while the tumor cells in the group without adding the invented composition can proliferate infinitely, entering exponential phase of growth, half inhibiting concentration of test group and control group are shown in table15Table 15.

Table 15.   Half inhibiting concentration of the invented composition and canelim capsule on tumor cell

30   growth

(IC$_{50}$, $\bar{x}\pm$SD   n=3)

Cell line	Invented composition (mg/ml)	Canelim capsule (mg/ml)
Hela	4.06±1.92	5.35±2.19
Al	2.12±0.41	5.51±2.47

15

The invented composition has inhibition effects on vitro cultured human tumor cells (Hela、Al), half inhibiting concentration (IC_{50}) is about 2-5mg/ml.

Test example 3 Acute toxicity test of the invented Traditional Chinese Medicine composition

5   Ⅰ.Tested drugs

1. Preparation labeled dosage: 1 ml containing 0.55g of crude drug.

2. Preparative methods: stock solution was diluted to demanding concentration with sterile purified water.

3.Solvent: sterile purified water

10   Ⅱ.Animal :mice

1. Kunming mice, supplied by animal center, Shanghai institute of pharmaceutical industry

2. Weight: 20±1g, 6−7 weeks old.

3. Mice number:20 mice each group(10 male mice and 10 female mice)

Ⅲ. Test Methods

15   1. Administration manner: ip

2. Dosage group: 5 groups, calculation unit ml/kg.

3. Volume: 0.5ml per mouse.

4. Solvent: sterile purified water

5. Mice abnormal reactions: Mice immediately appear abdomen intense contraction, body stretching and

20   twist, rebound, short of breath, then mice show action retardation, hair looseness, death appears 1 hour after administration, death climax appears 6 hours after administration. Individual mouse dies 3 days after administration (shown in ~~table16~~Table 16), dissecting dead mice, only mesentery congestion, lots of drug residues in abdominal cavities can be observed by naked eyes. Observing for 3 weeks, calculating LD50 with Bliss method.

25

6. Results

Ip×1 LD50 of the invented Traditional Chinese Medicine composition is shown in ~~table16~~Table 16. It demonstrates that LD_{50} of the invented Traditional Chinese Medicine composition on Kunming mice has no significant difference between male and female mice (P>0.05) (See ~~table17~~Table 17).

30

Table 16. Animal death distribution of acute toxicity of the invented composition via ip

sex	dosage	mice number	death distribution（date)	death rate	LD_{50} （95% confidence limit)

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	ml/kg		1	2	3	4	5	6	7......21	%	ml/kg
	25	10	9	1	0	0	0	0	0	100	
	20	10	5	3	0	0	0	0	0	80	
male	16	10	2	1	0	1	0	0	0	40	16.7（15.2—18.36）
	12.8	10	0	1	0	0	0	0	0	10	
	10.24	10	0	0	0	0	0	0	0	0	
	25	10	10	0	0	0	0	0	0	100	
	20	10	5	2	0	0	0	0	0	70	
female	16	10	3	1	0	0	0	0	0	40	17.08（15.47—18.86）
	12.8	10	0	1	0	0	0	0	0	10	
	10.24	10	0	0	0	0	0	0	0	0	

Table 17. Acute toxicity test results of the invented composition on mice via ip administration

sex	LD_{50}	LD_5	LD_{95}
	ml/kg		（95％confidence limit）
male	16.7 （15.2—18.36）	12.27 （10.34—14.56）	22.71 （19.12—26.97）
female	17.08 （15.47—18.86）	12.19 （10.17—14.62）	23.91 （19.87—28.77）
male and female	16.89 （15.77—18.09）	12.23 （10.79—13.85）	23.32 （20.55—26.46）

6.Conclusion

Acute toxicity LD50 of the invented composition on mice via ip administration is 16.89ml/kg, which is equal to 9.29g/kg of crude drug.

Application example_1 Summary of clinical trail of the invented composition on the treatment of primary hepatic carcinoma and gastric cancer

Object and method

I . Choice of eligible tested object

1. Chinese medicine syndrome diagnosis symptom of stagnation of poison

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Gastric cavity full, hard lump, Stabbing pain, loss of appetite, fatigue, vomit, haematemesis, hemafecia, dark , dark red, purple, cyanochroia or ecchymosis texture of tongue, white or yellow coated tongue, extenuated, deep or astringent pulse.

2. Western medical ~~diagosis~~ diagnosis criterion:

5   Primary hepatic carcinoma

　　　1) pathologic diagnosis

　　　(1)Liver histological examination proved to be primary hepatic carcinoma

　　　(2) Histologic examination of extra-hepatic tissue proved to be primary hepatic carcinoma

　　　2) Clinical diagnosis

10　　　(1)　If there is no other evidence of hepatic carcinoma, AFP positive by convection method check or AFP ≥400ng/ml by radioimmunity method check, and persistent more than 4 weeks, excluding pregnancy, reactive hepatopathy, gonadal embryonal tumor and metastatic hepatic carcinoma.

　　　　(2)　Have or have no clinical manifestation, B ultrasonic check and CT examination show definite intrahepatic parenchymatous occupying lesion, excluding hemangiomas of liver and metastatic hepatic

15　　　　carcinoma., plus any one of the followings:

　　　　　① AFP≥200ng/ml or obviously high γ -GT.

　　　　　②　Imageological manifestation of typical primary hepatic carcinoma.

　　　　　③ No jaundice, but obviously high AKP or γ -GT.

　　　　　④ Obvious metastasis in distant area, bloody ascites or finding cancer cells in the ascites.

20　　　　　⑤ Definite cirrhosis with type B hepatitis marker positive.

　　　3) Clinical stage criterion

　　　Ⅰ : No definite symptoms and signs of hepatic carcinoma, CT、B ultrasonic examination finds single node, size less than 5cm.

　　　Ⅱ : Mild symptom, good general condition, exceeds criterion of stage Ⅰ , while there is no evidence of stage

25　　　Ⅲ: any one of obvious cachexia, jaundice, ascites or extrahepatic metastasis

　　　Gastric carcinoma

　　　(1) Medical history and symptom: no symptom at earlier period, male, >40, epigast discomfort for unknown reasons, pain, progressing anemia and emaciation, or regularity of ulcer changed, loss of appetite, vomit, haematemesis or hemafecia.

30　　　(2) Sign: epigast tenderness or lump palpable, at advantaged stage, superficial lymphadenectasis can be palpable, hard, ascites, anemia.

　　　(3) Fecal occult blood test:　Fecal occult blood test shows positive for consecutive 3 days.

　　　(4) Gastric fluid analysis:　gastric fluid decrease or hypchlorhydia.

　　　(5) Upper gastrointestinal opacification: dysperistalsis, destroy of gastric ~~mucos~~ mucus, changing of gastric

emptying time (acceleration or retardation), abnormality of gastric contour, niche sign of irregular margin and filling defect.

(6) Gastric endoscope examination: tumor or large irregular ulcer can be visible.

(7) Exfoliative cytometer examination of gastric fluid: finding out typical cancer cells.

5　(8) Operation pathologic sample, biopsy of superficial lymph nodes, endoscope pathologic sample substantiated cases.

Clinical stage criterion of gastric carcinoma

Ⅰ: Superficial carcinoma with no lymph nodes metastasis and tumor infiltrated into less than 1/2 sector of the muscular layer.

10　Ⅱ: Superficial carcinoma with first station lymph nodes metastasis and carcinoma infiltrated into muscular layer, exceeded 1 sector, and T_3 tumor without or only with adjacent lymph nodes metastasis.

Ⅲ: Regardless of tumor size, tumor with distant superficial lymph nodes metastasis or with adjacent deep lymph nodes metastasis, or tumor only with adjacent superficial lymph nodes metastasis, even without lymph nodes metastasis, but the size of the tumor exceeded 1 sector of muscular layer or

15　infiltrated into surrounding tissues.

Ⅳ: Regardless of tumor size, tumor with distant metastasis or metastasis of hepatic hilum lymph nodes,para- arteria coeliaca lymph nodes, paraaortic lymoh lumph nodes, para- arteria colica media lymph nodes or lymph nodes of root of mesentery.

1. Inclusion criterion

20　(1) Stage Ⅰ,Ⅱ patients are reluctant to receive other treatments, participating clinical trails voluntarily.

(2) Those patients who have received anti-cancer therapy(including total chemotherapy, arterial cannula chemotherapy and embolotherapy), partly radiotherapy, operations(excluding patients who relapsed after surgical radical correction), cryotherapy or injecting with absolute alcohol, need stop therapy for over 3 months.

25　(3) Age>18 years

(4) Predicted survival time>2 months, survival quality Karnofsky score≥50

2. Excluding Case Criterion

(1) Age < 18 years

(2) Pregnant or breast-feeding women.

30　(3) Patients with esophageal stenosis, polypi or tumor; gastroduodenal ulcer; reactive gastritis, atrophic gastritis, bile reflux gastritis; bowel obstruction; structural diseases of liver, cholecyst, pancreas, colon; patients can not receive medication via po.

(4) Signs of gastric perforation or bleeding.

(5) Combined heart, liver, kidney and hematopoietic system, immune system severe primary diseases,

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psychotic patients.

(6) Those who refuse therapy.

(7) Be considered as those are unsuitable for participating in clinical trail by researchers.

II. Methods of clinical trails

5　1. Trail design:

According to Investigational New Drug Application(IND), performing clinical trails with the invented Traditional Chinese Medicine composition on treatment of primary hepatic carcinoma and gastric carcinoma, primary hepatic carcinoma cases are no less than 30 cases, gastric carcinoma cases are no less than 30 cases, without setting controls, in order to substantiate its anti-cancer effects.

10　2. Adiministration manner and dosage:

The invented Traditional Chinese Medicine composition, taken orally, twice each day, 15ml each time(1 ml containing crude drugs 0.75g), taken in the early morning and evening, taken with warm water.

3. Course of treatment: 2 months.

4. Observed items and methods

15　(1) Safety detection: blood, urine, faeces routine check; liver, kidney function, ECG are checked before and after therapy. In clinical trails, observe carefully the adverse reactions which may be caused by the invented composition, such as symptoms of digest, respiration, circulation, nerve and blood systems.

(2) Estimation of therapeutic efficacy:

20　①Tumor foci: performing B ultrasonic, CT or/and MRI examination before and after treatment.

a Measurement of tumor foci size: multiply the two perpendicular maximum diameter.

b Multiple tumor foci are measured with sum of all products of multiplication (refer to product of two perpendicular maximum diameter).

c Diffused nodular tumor should be explained particularly.

25　d Recording with or without portal vein cancer cell embolism.

②Clinical symptom observations:

a Main symptoms of primary heparic and gastric carcinoma:

Hepatic region pain, lump in superior belly, fatigue, emaciation, jaundice and fever.

b Main symptoms of stagnation of poison:

30　Lump below the costal region, ~~discomfortableness~~ uncomfortableness and pain, fever, dry mouth and bitter mouth, dry stool, constipation, body or eyestained yellow, dark red, purple or cyanochroia texture of tongue, yellow coated tongue, astrigent pulse.

c Survival quality: Karnofsky grade

d Other examination items: AFP、AKP、γ-GT、CD3、CD4、CD8 etc.

20

Observing methods:

Observing methods: observing and recording symptoms, Karnofsky score, tongue and pulse regularly; Laboratory examination items including blood routine test, bleeding time and clotting time are checked once a week during or after treatment; urine routine test, faeces routine test, AFP, γ—GT,LDH, liver function and kidney function are checked once two weeks during or after treatment; Immunology index, ECG, heart function, chest X-Ray are checked once four weeks during or after treatment; the Examination of imageology is carried on once eight weeks during or after treatment, the examination can be carried on at any time when needed.

Ⅲ Therapeutic efficacy assessment criterions

1.Therapeutic efficacy assessment criterions of the tumor foci:

(1) Complete Remission(CR): tumor disappeared and maintained for more than 1 month.

(2) Partial Remission(PR): product of two maximum diameters of tumor minimized more than 50%, and maintained for more than 1 month.

(3)**Stable disease** (SD): product of two maximum diameters minimized less than 50%, increased by no more than 25%, maintained for more than 1 month.

(4)Progression disease(PD): product of two maximum diameters increased by more than 25%.

Total remission rate=CR+PR

1. survival quality assessment criterions:

According to Karnofsky score criterions, it is compared before and after treatment.

Karnofsky score criterions:

Normal, no discomfort or sign of disease	100
Normal activity, mild sign of disease	90
Nearly normal activity, certain symptoms or signs	80
Self care, can not maintain normal activity and work	70
Life need help occasionally, but can meet most individual demands	60
Need many help and medical care	50
Losing living abilities, need special help and care	40
Losing living abilities severely, need treatment in hospital, no death threat temporarily	30
Badly ill, need to be kept in hospital and given powerful Supportive treatment	20
In great danger	10
Death	0

Ⅳ. Handling and summarizing of clinical trail data

Collecting all data, inputing inputting the medical history into computers, constructing database using EPI

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INF06 software, making statistical treatment and analysis, writing summary of clinical trails, making objective assessment about clinical therapeutic effects and safety of the invented Traditional Chinese Medicine composition treatment on primary hepatic carcinoma and gastric carcinoma.

Results

5   100 eligible cases, all belong to group treated with the invented composition solely; Of which 41 cases of primary hepatic carcinoma, 59 cases of gastric carcinoma diagnosed by western medicine, while being considered as the symptom of stagnation of poison

I .General condition

1. Sex

10

Table 1   sex construction

	male	female	total
Primary hepatic carcinoma	33	8	41
Gastric carcinoma	44	15	59

2. Age

Table 2   age block

	34-40	41-50	51-60	61-78	$\Box x \pm SD$
Primary hepatic carcinoma	6	10	12	13	53.9±10.2
Gastric carcinoma	4	14	13	28	56.5±9.5

3. course of disease

Table 3 course of disease (month)

	case*	1-3	4-6	7-12	13-50
Primary hepatic carcinoma	36	26	3	4	3
Gastric carcinoma	57	21	10	12	14

15   ●   data of 5 cases of primary hepatic carcinoma and 2 cases of gastric carcinoma are lost.

4. Past treatment

Table 4   past treatment*

	case*	untreated	operation	TCM	TAI
Primary hepatic carcinoma	40	27	6	2	5
gastric carcinoma	58	26	17	3	12

* data of 1 case of primary hepatic carcinoma and 1 case of gastric carcinoma are lost

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5. Foci type and location

Among 41 cases of primary hepatic carcinoma, massive type, nodular type and diffuse type are 17 cases (41.5%) ,17 cases (41.5%) and 7 cases (17.1%) respectively, 3 cases (7.3% of tumors located in left hepatic lobe, 29 cases (70.7%) of tumors located in right hepatic lobe, 9 cases (22%) of tumors located in both lobes.

Among 59 cases of gastric carcinoma, carcinoma located in upper region, middle region , lower region or other regions of stomach are 4 cases (6.8%) , 8 cases (13.6%) , 18 cases (30.5%) , 21cases(35.6%)respectively, 7 cases(11.9 %) of carcinoma located in multiple regions of stomach.

6. Clinical stage

Table 5　　clinical stage

	cases	包I	包II	包III	包IV
Primary hepatic carcinoma	41	2	20	19	0
Gastric carcinoma	59	1	1	19	37

7. Karnofsky score before treatment

Table 6　　Karnofsky score before treatment

	cases	50-69	70-79	80-90	$\bar{x} \pm s$
Primary hepatic carcinoma	41	9	21	11	69.8±13.9
Gastric carcinoma	59	24	27	8	65.9±8.9

8. Body weight before treatment

Table 7　　Body weight (kg) before treatment

	cases	36-50	51-60	61-70	71-76	$\bar{x} \pm s$
Primary hepatic carcinoma	41	3	15	20	3	61.0±7.9
Gastric carcinoma	59	13	26	13	4	56.4±8.8

9. Appetite before treatment

Table 8　　appetite before treatment (taels/day)

	cases	1-4	4-5.9	6-7.9	8-12	$\bar{x} \pm s$
Primary hepatic carcinoma	41	9	12	13	7	5.7±1.6
Gastric carcinoma	59	19	8	24	6	5.3±1.9

* data of 1 case of gastric carcinoma are lost.

10. AFP test before treatment of primary hepatic carcinoma

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Table 9   AFP （ug/ml） test before treatment of primary hepatic carcinoma

	cases	<30	30-399	≥400	$\overline{x} \pm s$
primary hepatic carcinoma	39	2	3	34	381.69±126.13

11. γ-GT test before treatment of primary hepatic carcinoma

Table 10   γ-GT test before treatment of primary hepatic carcinoma

	cases	$\overline{x} \pm s$ (n)
primary hepatic carcinoma	22	200.2±103.7 （22）

II.Therapeutic efficacy

1.Total efficacy

Table 11 total therapeutic efficacy

disease	cases*	CR(%)	PR(%)	SD(%)	PD(%)
primary hepatic carcinoma	41	0(0.0%)	1(2.4%)	34(82.9%)	6(14.6%)
Gastric carcinoma	59	0(0.0%)	6(10.2%)	49(83.0%)	4(6.8%)

CR,PR,SD,PD of primary hepatic carcinoma after treatment are 0, 2.4%, 82.9%, 14.6% respectively.

CR,PR,SD,PD of gastric carcinoma after treatment are 0, 10.2%, 83.0%, 6.8% respectively.

2. Follow-up life span, survival rate after treatment

Table 12   Deaths 8 weeks after treatment

disease	cases	survival	death （cause）				
			hepatic coma	hepatorrhexis	upper gastrointestinal bleeding	failure	others
primary hepatic carcinoma	41	39	0	0	0	1	1
gastric carcinoma	59	45	0	0	1	12	1

Table 13   Deaths 1.5 year after treatment

disease	cases	survival	death （cause）

			hepatic coma	Hepatorrhe-xis	upper gastrointestinal bleeding	failure	hepatorenal syndrome	others
primary hepatic carcinoma	41	8	5	4	8	10	2	4
Gastric carcinoma	59	25	0	0	3	28	0	3

Table 14   life span(month), survival rate 1.5 years after treatment（Ⅰ）

disease	cases	Complete data cases	censored	%censored
primary hepatic carcinoma	41	33	8	19.5%
Gastric carcinoma	59	34	25	42.4%

Table 15   life span(month), survival rate 1.5 years after treatment（Ⅱ）

disease	cases	Average survival time(month) $\overline{x} \pm se$	Median Survival Time (month) $\overline{x} \pm se$	1 year survival rate %	standard error
primary hepatic carcinoma	41	7.7±0.9	5.0±1.3	16.5	6.0
Gastric carcinoma	59	10.7±0.8	11.0±1.5	33.0	7.7

3. Comparison of changes of tumor foci size before and after treatment

Table 16 Comparison of changes of tumor foci size$^{\$}$ before and after treatment

disease	before treatment $\overline{x} \pm s$ (n)	after treatment $\overline{x} \pm s$ (n)	difference（after-before） $\overline{x} \pm s$ (n)
primary hepatic carcinoma	39.4±42.9(37)	46.5±53.1(36)	6.4±29.6(36)[*]
Gastric carcinoma	19.2±21.1(59)	15.8±14.4(59)	-3.4±12.0(59)[#]

$ Size of tumor foci：product of two perpendicular maximum diameters or sum of products of multiple foci（cm×cm）。

*Primary hepatic carcinoma, t=1.30, P=0.203

Gastric carcinoma, t=2.17, P=0.034

For Primary hepatic carcinoma patients, there is no notable significance in the difference of tumor foci size before and after treatment

5   For Gastric carcinoma patients, there is notable significance in the difference of tumor foci size before and after treatment.

4. Changes of Karnofsky score after treatment

Table 17 Changes of Karnofsky score after treatment

disease	before treatment	after treatment	difference (after-before)
	$\bar{x} \pm s$ (n)	$\bar{x} \pm s$ (n)	$\bar{x} \pm s$ (n)
Primary hepatic carcinoma	69.8±13.9(41)	78.1±8.7(31)	7.7±16.1(31)*
Gastric carcinoma	65.9±8.9(59)	77.1±9.9(56)	11.6±8.0(56)#

* Primary hepatic carcinoma, t=2.68, P=0.012

10   # Gastric carcinoma, t=10.80, P=0.000

For Primary hepatic carcinoma patients, there is notable significance in the difference of Karnofsky score before and after treatment

For Gastric carcinoma patients, there is notable significance in the difference of Karnofsky score before and after treatment

15   5. Changes of body weight after treatment

Table 18 Changes of body weight after treatment (Kg)

disease	before treatment	after treatment	difference (after-before)
	$\bar{x} \pm s$ (n)	$\bar{x} \pm s$ (n)	$\bar{x} \pm s$ (n)
Primary hepatic carcinoma	61.0±7.9(41)	63.1±7.3(31)	0.9±1.4(31)*
Gastric carcinoma	56.4±8.8(59)	56.9±8.3(55)	1.0±3.6(52)#

*Primary hepatic carcinoma ,t=3.50, P=0.001

Gastric carcinoma, t=2.10, P=0.040

For Primary hepatic carcinoma patients, there is notable significance in the difference of body weight

20   before and after treatment

For Gastric carcinoma patients, there is notable significance in the difference of body weight before and after treatment,

6. Changes of appetite after treatment

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Table 19   Changes of appetite after treatment（taels/day）

disease	before treatment	after treatment	difference（after-before）
	$\overline{x} \pm s$ (n)	$\overline{x} \pm s$ (n)	$\overline{x} \pm s$ (n)
primary hepatic carcinoma	5.7±1.6(41)	6.7±1.5(31)	1.2±1.4(31)[*]
gastric carcinoma	5.3±1.9(59)	6.7±2.7(58)	1.5±1.7(56)[#]

* Primary hepatic carcinoma，t=4.77，P=0.000

Gastric carcinoma，t=6.47，P=0.000

For Primary hepatic carcinoma patients, there is notable significance in the difference of appetite before and after treatment.

For Gastric carcinoma patients, there is notable significance in the difference of appetite before and after treatment.

7. Improvements of symptoms and signs after treatment

Table 20   Improvement of fatigue after treatment[*]

disease	cases	aggravation	no change	Improved 1 grade	Improved 2 grades	Improved 3 grades
Primary hepatic carcinoma	30	1	14	7	8	0
Gastric carcinoma	58	2	20	19	10	7

* Data of 11 cases of primary hepatic carcinoma and 1 case of gastric carcinoma are lost

Improved 1 grade: lowered 1 grade after treatment compared with before treatment, for example, fatigue is difficult to recover after activities, while it is improved to be easy to recover post-treatment.

Improved 2 grades : lowered 2 grades after treatment compared with before treatment, for example, feeling fatigue when rest, while post-treatment fatigue is easy to recover after activities.

Improved 3 grades: lowered 3 grades after treatment compared with before treatment, for example, Lying in bed, while post-treatment fatigue is easy to recover after activities.

For primary hepatic carcinoma patients, improvement rate of fatigue is 50.0%.

For gastric carcinoma patients, improvement rate of fatigue is 62.1%.

8. Improvements of symptoms and signs after treatment

Table 21 improvement of epigastralgia (gastric carcinoma) after treatment

disease	cases	aggravation	no change	Improved 1 grade	Improved 2 grades	Improved 3 grades

27

gastric carcinoma	55	3	14	18	16	4

* Data of 4 cases of gastric carcinoma are lost.

Improvement rate of epigastralgia is 69.1%

Table 22   improvement of appetite after treatment (gastric carcinoma patients)[*]

disease	cases	aggravation	no change	Improved 1 grade	Improved 2 grades	Improved 3 grades
gastric carcinoma	55	3	21	16	12	3

* Data of 4 cases of gastric carcinoma are lost.

5   Improvement rate of appetite after treatment is 56.4% .

Table 23 improvement of dry mouth and thirsty after treatment[*]

disease	cases	aggravation	no change	Improved 1 grade	Improved 2 grades	Improved 3 grades
primary hepatic carcinoma	31	0	20	8	2	1
gastric carcinoma	58	1	44	9	4	0

*Data of 10 cases of primary hepatic carcinoma and 1 case of gastric carcinoma are lost

Improved 1 grade: thirst lowered 1 grade after treatment, for example, dry mouth and throat, no desire for

10   drink, improved to only dry mouth after treatment.

Improved 2 grades: thirst lowered 2 grades after treatment, for example, dry mouth and throat, desire for

drink, improved to only dry mouth.

Improved 3 grades: thirst lowered 3 grades after treatment, for example, dry mouth and sore throat,

improved to only dry mouth.

15   For primary hepatic carcinoma patients, improvement rate of thirst is 35.5%.

For gastric carcinoma patients, improvement rate of thirst is 22.4%.

Table 24   Improvement of bitter mouth after treatment

disease	cases	aggravation	no change	Improved 1 grade	Improved 2 grades	Improved 3 grades
primary hepatic carcinoma	31	0	20	10	1	0
gastric carcinoma	57	0	45	9	3	0

* Data of 10 primary hepatic carcinoma patients and 2 cases of gastric carcinoma are lost

20   For primary hepatic carcinoma patients, improvement rate of bitter mouth is 35.5%.

For gastric carcinoma patients, improvement rate of bitter mouth is 21.1%.

28

Table 25   Improvement of spontaneous perspiration after treatment[*]

disease	cases	aggravation	no change	Improved 1 grade	Improved 2 grades	Improved 3 grades
primary hepatic carcinoma	31	0	24	5	1	1
gastric carcinoma	57	2	42	8	5	0

*Data of 10 cases of   primary hepatic carcinoma and 2 cases of gastric carcinoma are lost.

Improved 1 grade: spontaneous perspiration lowered 1 grade after treatment, for example, perspire immediately after activities, improved to perspire occasionally after activities.

Improved 2 grades: spontaneous perspiration lowered 2 grades after treatment, for example, perspire when rest, improved to perspire occasionally after activities.

Improved 3 grades: spontaneous perspiration lowered 3 grades after treatment, for example, perspire vehemently, improved to perspire occasionally after activities.

For primary hepatic carcinoma patients, improvement rate of spontaneous perspiration is 22.6%.

For gastric carcinoma patients, improvement rate of spontaneous perspiration is 22.8%.

Table 26   Improvement of night sweat after treatment[*]

disease	cases	aggravation	no change	Improved 1 grade	Improved 2 grades	Improved 3 grades
primary hepatic carcinoma	31	0	24	7	0	0
gastric carcinoma	57	3	44	5	4	1

*Data of 10 cases of primary hepatic carcinoma and 2 cases of gastric carcinoma are lost.

Improved 1 grade : night sweat lowered 1 grade after treatment, for example, night sweat usuaallyusually, improved to night sweat occasionally.

Improved 2 grades: night sweat lowered 2 grades after treatment, for example, night sweat every night, improved to night sweat occasionally.

Improved 3 grades: night sweat lowered 3 grades after treatment, for example, night sweat can wet cloth, improved to night sweat occasionally.

For primary hepatic carcinoma patients, improvement rate of night sweat is 22.6%.

For gastric carcinoma patients, improvement rate of night sweat is 15.8%.

Table 27   Improvement of upset and tantrum after treamenttreatment[*]

disease	cases	aggravation	no change	Improved 1 grade	Improved 2 grades	Improved 3 grades

29

primary hepatic carcinoma	31	0	26	5	0	0
gastric carcinoma	57	2	37	15	3	0

* Data of 10 cases of primary hepatic carcinoma and 2 cases of gastric carcinoma are lost.

Improved 1 grade: upset and tantrum lowered 1 grade after treatment, for example, upset and self-uncontrollable, improved to be upset and self-controllable.

Improved 2 grades: upset and tantrum lowered 2 grades after treatment, for example, burning sensation of five centres and tantrum, improved to be upset and self-controllable.

For primary hepatic carcinoma patients, improvement rate of upset and tantrum is 16.1%.

For gastric carcinoma patients, improvement rate of upset and tantrum is 31.6%.

Table 28 Improvement of dizziness after treatment[*]

disease	cases	aggravation	no change	Improved 1 grade	Improved 2 grades	Improved 3 grades
primary hepatic carcinoma	31	1	26	4	0	0
gastric carcinoma	57	3	36	14	4	0

* Data of 10 cases of primary hepatic carcinoma and 2 cases of gastric carcinoma are lost.

Improved 1 grade: dizziness lowered 1 grade after treatment, for example, dizzy usually, improved to dizzy occasionally.

Improved 2 grades: dizziness lowered 2 grades after treatment, for example, dizzy persistently, improved to dizzy occasionally.

For primary hepatic carcinoma patients, improvement rate of dizziness is 12.9%.

For gastric carcinoma patients, improvement rate of dizziness is 31.6%.

Table 29 Improvement of jaundice after treatment[*]

disease	cases	aggravation	no change	Improved 1 grade	Improved 2 grades	Improved 3 ~~grade~~gra des
primary hepatic carcinoma	31	2	28	1	0	0
gastric carcinoma	57	0	57	0	0	0

* Data of 10 cases of primary hepatic carcinoma and 2 cases of gastric carcinoma are lost.

Improved 1 grade: jaundice lowered 1 grade after treatment, for example, albuginea oculi and skin stained yellow, improved to only albuginea oculi mildly stained yellow.

For primary hepatic carcinoma patients, improvement rate of jaundice is 3.2%.

30

For gastric carcinoma patients, improvement rate of jaundice is 0%.

Table 30   Improvement of cancer pain after treatment[*]

disease	cases	aggravation	no change	Improved 1 grade	Improved 2 grades	Improved 3 grades
primary hepatic carcinoma	31	1	14	8	7	1
gastric carcinoma	57	1	35	12	8	1

*Data of 10 cases of primary hepatic carcinoma and 2 cases of gastric carcinoma are lost.

Improved 1 grade: cancer pain lowered 1 grade after treatment, for example, moderate cancer

5   pain(bearable, no upset), improved to mild cancer pain(discomfort, no upset)

Improved 2 grades: cancer pain lowered 2 grades after treatment, for example, severe cancer pain(active

body position,demand for painkiller), improved to mild cancer pain (discomfort, no upset)

Improved 3 grades: cancer pain lowered 3 grades after treatment, for example, uncontrollable pain(upset,

passive position, need painkiller to relieve),. improved to mild cancer pain(discomfort, no upset)

10   For primary hepatic carcinoma patients, improvement rate of cancer pain is 51.6%.

For gastric carcinoma patients, improvement rate of cancer pain is 36.8%.

Table 31   Improvement of abdominal distension after treatment[*]

disease	cases	aggravation	no change	Improved 1 grade	Improved 2 grades	Improved 3 grades
primary hepatic carcinoma	31	1	16	10	3	1
gastric carcinoma	57	0	26	19	10	2

* Data of 10 cases of primary hepatic carcinoma and 2 cases of gastric carcinoma are lost.

Improved 1 grade: abdominal distension lowered 1 grade after treatment, for example, abdominal

15   distension, unrelieved after passage of gas by anus, improved to relief after passage of gas by anus after

treatment, no ascites.

Improved 2 grades: abdominal distension lowered 2 grades after treatment, for example, obvious

abdominal distension with small or moderate volume of ascites, improved to abdominal distension, relief

after passage of gas by anus, no ascites after treatment.

20   Improved 3 grades: abdominal distension lowered 3 grades after treatment, for example, obvious

abdominal distension with large volume of ascites, improved to abdominal distension , relief after passage

of gas by anus, no ascites after treatment.

For primary hepatic carcinoma patients, improvement rate of abdominal distension is 45.2%.

For gastric carcinoma patients, improvement rate of abdominal distension is 54.4%.

25   Table 32   Improvement of diarrhea after treatment[*]

disease	cases	aggravation	no	Improved	Improved	Improved

31

			change	1 grade	2 grades	2 grades
primary hepatic carcinoma	31	0	26	2	3	0
gastric carcinoma	57	2	54	1	0	0

* Data of 10 cases of primary hepatic carcinoma and 2 cases of gastric carcinoma are lost.

Improved 1 grade: diarrhea lowered 1 grade after treatment, for example, bearable (>2d), improved to diarrhea transiently (<2d) after treatment.

Improved 2 grades: diarrhea lowered 2 grades after treatment, for example, unbearable diarrhea , improved to diarrhea transiently (<2d) after treatment.

For primary hepatic carcinoma patients, improvement rate of diarrhea is 16.1%.

For gastric carcinoma patients, improvement rate of diarrhea is 1.8%.

9. Disappearance of main symptoms and signs after treatment

Table 33   Disappearance of main symptoms after treatment

symptoms	disease	total cases	beginning cases	disappeared cases	disappearance rate
fatigue	primary hepatic carcinoma	31	26	10	61.5%
	gastric carcinoma	58	50	18	36.0%
dry mouth	primary hepatic carcinoma	31	20	7	35.0%
and thirst	gastric carcinoma	58	17	11	64.7%
bitter mouth	primary hepatic carcinoma	31	15	9	60.0%
	gastric carcinoma	58	13	9	69.2%
spontaneous	primary hepatic carcinoma	30	12	6	50.0%
perspiration	gastric carcinoma	58	17	10	58.8%
night sweat	primary hepatic carcinoma	31	13	7	53.8%
	gastric carcinoma	58	12	10	83.3%
upset and	primary hepatic carcinoma	31	10	5	50.0%
tantrum	gastric carcinoma	58	20	15	75.0%
dizziness	primary hepatic carcinoma	31	7	3	42.9%
	gastric carcinoma	58	24	14	58.3%
jaundice	primary hepatic carcinoma	31	10	1	10.0%
	gastric carcinoma	58	2	0	0%
cancer pain	primary hepatic carcinoma	31	23	13	56.5%
	gastric carcinoma	58	30	14	46.7%
	primary hepatic carcinoma	31	27	10	37.0%

32

abdominal distension	primary hepatic carcinoma	31	27	10	37.0%
abdominal distension	gastric hepatic carcinoma	57	45	55	39.0%
	gastric carcinoma	58	3	1	33.3%

* Data of 10 or 11 cases of primary hepatic carcinoma and 1 or 2 cases of gastric carcinoma are lost.

10. Changes of White Blood Cells(WBC) after treatment

Table 52 Changes of White Blood Cells(WBC) after treatment*

disease	cases	aggravation	no change	Improved 1 grade	Improved 2 grades	Improved 3 grades
primary hepatic carcinoma	29	3	25	1	0	0
gastric carcinoma	55	2	50	1	0	2

5   * Grade WBC accurately according to "WHOgrade ~~erterions~~ criterions for acute and subacute toxicity reactions of the anti-caner drugs"..

Aggravation: WBC grade increased more than 1 grade after treatment compared with before treatment

Improved 1 grade: WBC grade lowered 1 grade after treatment compared with before treatment.

Improved 2 grades: WBC grade lowered 2 grades after treatment compared with before treatment.

10   Improved 3 grades: WBC grade lowered 3 grades after treatment compared with before treatment.

For primary hepatic carcinoma patients, improvement rate of WBC is 3.5%, aggravation rate of WBC is 10.3%.

For gastric carcinoma patients, improvement rate of WBC is 5.5%, aggravation rate of WBC is 3.6%.

15   11. Changes of granulocytes after treatment

Table 35   Changes of granulocytes number after treatment*

disease	cases	aggravation	no change	Improved 1 grade	Improved 2 grades	Improved 3 grades
primary hepatic carcinoma	17	0	15	2	0	0
gastric carcinoma	53	1	52	0	0	0

*~~Gradie~~ Grade granulocytes number accurately according to "WHO grade ~~eriteriions~~ criterions for acute and subacute toxicity reactions of the anti-cancer drugs".

Aggravation: granulocytes number grade increased more than 1 grade after treatment compared with

20   before treatment

33

Improved 1 grade: granulocytes number grade lowered 1 grade after treatment compared with before treatment.

Improved 2 grades: granulocytes number grade lowered 2 grades after treatment compared with before treatment.

5 Improved 3 grades: granulocytes number grade lowered 3 grades after treatment compared with before treatment.

For primary hepatic carcinoma patients, improvement rate of granulocytes number is 11.8%, aggravation rate of granulocytes number is 0%.

For gastric carcinoma patients, improvement rate of granulocytes is 0%, aggravation rate of granulocytes

10 number is 1.9% .

12. Changes of hemoglobin number after treatment

Table 36 Changes of hemoglobin number after treatment[*]

disease	cases	aggravation	no change	Improved 1 grade	Improved 2 grades	Improved 3 grades
primary hepatic carcinoma	31	5	24	2	0	0
gastric carcinoma	55	9	36	8	1	1

*Grade hemoglobin number accurately according to "WHOgrade criterions for acute and subacute toxicity

15 reactions of the anti-cancer drugs".

Aggravation: hemoglobin number grade increased more than 1 grade after treatment compared with before treatment

Improved 1 grade: hemoglobin number grade lowered 1 grade after treatment compared with before treatment.

20 Improved 2 grades: hemoglobin number grade lowered 2 grades after treatment compared with before treatment.

Improved 3 grades: hemoglobin number grade lowered 3 grades after treatment compared with before treatment.

For primary hepatic carcinoma patients, improvement rate of hemoglobin number is 6.5%, aggravation

25 rate of hemoglobin number is 16.1%.

For gastric carcinoma patients, improvement rate of hemoglobin number is 18.2% , aggravation rate of hemoglobin number is 16.4%.

13. Changes of platelets number after treatment

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Table 37 Changes of platelets number after treatment[*]

disease	cases	aggravation	no change	Improved 1 grade	Improved 2 grades	Improved 3 grades
primary hepatic carcinoma	29	1	25	3	0	0
gastric carcinoma	55	1	51	1	1	1

* Grading platelets number accurately according to "WHOgrade criterions for acute and subacute toxicity reactions of the anti-cancer drugs".

Aggravation: platelets number grade increased more than 1 grade after treatment compared with before treatment

Improved 1 grade: platelets number grade lowered 1 grade after treatment compared with before treatment.

Improved 2 grades: platelets number grade lowered 2 grades after treatment compared with before treatment.

Improved 3 grades: platelets number grade lowered 3 grades after treatment compared with before treatment.

For primary hepatic carcinoma patients, improvement rate of platelets number is 10.3%, aggravation rate of platelets number is 3.5%.

For gastric carcinoma patients, improvement rate of platelets number is 5.5%, aggravation rate of platelets number is 1.8%.

14. Comparison of immunologic index CD3 before and after treatment

Table 38 Comparison of immunologic index CD3 before and after treatment

disease	before treatment $\bar{x} \pm s$ (n)	after treatment $\bar{x} \pm s$ (n)	difference (after-before) $\bar{x} \pm s$ (n)
primary hepatic carcinoma	53.5±9.7(35)	55.9±9.8(25)	1.8±2.1(25)[*]
gastric carcinoma	60.2±12.7(29)	61.6±14.0(29)	1.3±9.2(29)[#]

* Primary hepatic carcinoma, t=4.18, P=0.000.

Gastric carcinoma, t=0.76, P=0.452.

For Primary hepatic carcinoma patients, there is notable significance in the difference of immunologic index CD3 before and after treatment.

For Gastric carcinoma patients, there is no notable significance in the difference of immunologic index CD3 before and after treatment.

15. Comparison of immunologic index CD4 before and after treatment

35

Table 39 Comparison of immunologic index CD4 before and after treatment

disease	before treatment	after treatment	difference(after-before)
	$\overline{x} \pm s$ (n)	$\overline{x} \pm s$ (n)	$\overline{x} \pm s$ (n)
primary hepatic carcinoma	34.7±5.0(35)	35.1±3.9(25)	1.4±1.4(25)*
gastric carcinoma	40.5±9.5(29)	37.9±8.4(29)	-2.6±5.4(29)#

*Primary hepatic carcinoma, t=5.23, P=0.000.

Gastric carcinoma, t=2.65, P=0.013.

For Primary hepatic carcinoma patients, there is notable significance in the difference of immunologic

5   index CD4 before and after treatment.

For Gastric carcinoma patients, there is notable significance in the difference of immunologic index

CD4 before and after treatment.

16. Comparison of immunologic index CD8 before and after treatment

Table 40 Comparasion of immunologic index CD8 before and after treatment

	before treatment	after treatment	difference (after-before)
	$\overline{x} \pm s$ (n)	$\overline{x} \pm s$ (n)	$\overline{x} \pm s$ (n)
primary hepatic carcinoma	30.2±5.8(35)	29.2±4.5(25)	-1.1±3.9(25)*
gastric carcinoma	31.2±8.1(29)	28.9±8.3(29)	-2.3±4.4(29)#

10   * Primary hepatic carcinoma, t=1.47, P=0.154.

Gastric carcinoma, t=2.75, P=0.010.

For Primary hepatic carcinoma patients, there is no notable significance in the difference of immunologic

index CD8 before and after treatment.

For Gastric carcinoma patients, there is notable significance in the difference of immunologic index

15   CD8 before and after treatment.

17. Comparison of immunologic index CD4/CD8 before and after treatment

Table 41   Comparison of immunologic index CD4/CD8 before and after treatment

	before treatment	after treatment	difference (after-before)
	$\overline{x} \pm s$ (n)	$\overline{x} \pm s$ (n)	$\overline{x} \pm s$ (n)
primary hepatic carcinoma	1.23±0.55(34)	1.25±0.35(25)	0.11±0.26(33)*
gastric carcinoma	1.35±0.44(29)	1.46±0.47(29)	0.00±0.31(29)#

* Primary hepatic carcinoma, t=2.20, P=0.037.

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Gastric carcinoma, t=1.51, P=0.145.

For Primary hepatic carcinoma patients, there is notable significance in the difference of immunologic index CD4/CD8 before and after treatment .

For Gastric carcinoma patients, there is no notable significance in the difference of immunologic index
5   CD4/CD8 before and after treatment.

18. Comparison of primary hepatic carcinoma γ-GT before and after treatment

Table 42   Comparison of primary hepatic carcinoma γ-GT before and after treatment

disease	before treatment	after treatment	difference(after-before)
	$\overline{x} \pm s$ (n)	$\overline{x} \pm s$ (n)	$\overline{x} \pm s$ (n)
primary hepatic carcinoma	200.2±103.7(22)	207.6±101.8(58)	-7.4±24.2(22)

t=1.437, P=0.165;

10

III.Results of imageology examination after treatment:

1. B type ultrasonic examination:

Totally there are 36 cases of primary hepatic carcinoma received B type ultrasonic examination, all show abnormalities, after treatment, rechecked and still show abnormalities. 37 cases of gastric
15   carcinoma patients received B type ultrasonic examination, of which, 17 cases are normal, 20 cases show abnormalities, rechecked after treatment, no obvious changes.

2. CT and MRI examinations

14 cases of primary hepatic carcinoma patients received CT or MRI examinations, 4 cases are normal, 10 cases are abnormal, rechecked after treatment, no obvious changes. 8 cases of gastric carcinoma
20   patients received CT or MRI examinations, all are abnormal, rechecked after treatment, 1 case is normal, 7 cases are abnormal.

IV. Safety Inspection

All safety indexs-indexes are normal before treatment, abnormalities appeared after treatment are
25   recorded in following table

doubtful adverse reaction	positive cases/total cases	incidence rate

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Hemoglobin number reduction	7/96	7.3%
RBC number reduction	3/93	3.2%
WBCnumber reduction	2/95	2.1%
Granulocytes number reduction	1/83	1.2%
Platelet number reduction	1/95	1.1%
Bilirubin increase	0/91	0.0%
AKP rising	2/94	2.1%
GPT rising	3/93	3.2%
BUN rising	1/94	1.1%
serum creatinine rising	0/94	0.0%
Abnormal urine protein	2/79	2.5%
Abnormal Abnormal urine RBC	5/79	6.3%
fecal occult blood	3/80	3.8%

六. Adverse event observations

During the courses of clinical trails, doubtful adverse reaction occurred to many cases, including fever, alopecie, choking, short of breath, non-cancer non-cancer pain, nausea and vomit, constipation and fecal occult blood, see details in following tables

doubtful adverse events	cases(n=100)	incidence rate
fever	7	7.0%
alopecie	1	1.0%
oral cavity ulcer	0	0.0%
cutaneous reaction	0	0.0%
choking and short of breath	2	2.0%
non cancer pain	3	3.0%
hypersensitiveness	0	0.0%
nausea and vomit	11	11.0%
constipation	22	22.0%
bleeding	3	3.0%

During the courses of treatment, doubtful adverse reaction occurred to some patients, such as fever, alopecie, choking, short of breath, non cancernon-cancer pain, nausea, vomit. constipation and bleeding,

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the incidence rate is shown in above table. For 36 cases, at least one doubtful adverse reaction appears , total incidence rate of doubtful adverse reaction is 36.0% (36/100) .

Conclusions

5   100 suitable cases, of which, 41 cases of primary hepatic carcinoma, 59 cases of gastric carcinoma, are considered as symptoms of stagnation of poison by Traditional Chinese Medicine.

CR, PR, SD and PD rate of treatment on primary hepatic carcinoma are 0, 2.4%, 82.9%, 14.6% respectively; CR, PR, SD and PD rate of treatment on gastric carcinoma are 0, 10.2%,83.0%, 6.8% respectively.

10   Results of 1.5 years follow-up after treatment show that 1 year survival rates of primary hepatic carcinoma patients and gastric carcinoma patients are 16.5% and 31.7% respectively, median life spans of primary hepatic carcinoma patients and gastric carcinoma patients are 5 months and 11 months respectively, average survival time are 7.7 months and 10.7 months respectively.

Gastric carcinoma patients enrolled into this clinical trails are mainly in advanced stage, of which, stage

15   III, 19 cases (32.2%); stage IV, 37 cases (62.7%) , above therapeutic efficacy on gastric carcinoma demonstrates that the invented Traditional Chinese Medicine composition has relative better effects on ~~gastic~~ gastric carcinoma (considered as symptom of stagnation of poison by Traditional Chinese ~~Medinine~~Medicine). PR rate is 10.2%, SD rate is 83.0%, 1 year survival rate is 31.7%, median life span is 11 months.

20   Results of solid tumor foci size assessment indicate:

Comparison of tumor foci size of primary hepatic carcinoma before and after treatment, there is notable significance in the difference.

Comparison of tumor foci size of gastric carcinoma before and after treatment, there is notable significance in the difference. Tumor foci size is minimized obviously after treatment, suggesting the

25   invented Traditional Chinese Medicine composition can minimize tumor foci when used to treat gastric carcinoma (considered as symptom of stagnation of poison by ~~Tradtional~~Traditional Chinese medicine)

Therapeutic effects on main symptoms demonstrate:

After treated with the invented Traditional Chinese Medicine composition, Karnofsky scores, body weights, appetites of the primary hepatic carcinoma patients and ~~gatric~~gastric carcinoma patients increased

30   obviously compared with before treatment. There is notable significance in their differences.

After treated with the invented Traditional Chinese Medicine composition, symptoms such as fatigue, dry mouth, thirst, dizziness, gastric ~~discomfortableness~~discomfort, loss of ~~apptite~~appetite, bitter taste of mouth, spontaneous perspiration, night sweat, upset, tantrum, choking, short of breath, cancer pain, abdominal distension, are all improved compared with before treatment.

39

Above results indicate that the invented Traditional Chinese Medicine composition can improve survival qualities of patients and ameliorate clinical symptoms of patients when used to treat primary hepatic carcinoma and gastric carcinoma (considered as ~~ymptom~~ symptom of stagnation of poison by ~~Traditonal~~ Traditional Chinese Medicine)

5 Results of laboratory examination show:

As to immunological index, Comparison results before and after treatment demonstrate that changes of CD3, CD4, CD4/CD8 of the primary hepatic carcinoma patients have significant difference; while CD4, CD8 of the gastric carcinoma patients are lower than those of before treatment, CD4/CD8 has no obvious changes. It suggests that the invented Traditional Chinese Medicine composition can enhance cellular

10 immune functions of primary hepatic carcinoma patients, while it may not enhance cellular immune functions of gastric carcinoma patients.

WBC, granulocytes, platelets of primary hepatic carcinoma patients and gastric patients have no obvious augmentations after treatment.

In summary, results of 100 cases of clinical trails without control demonstrate that the therapeutic effects

15 of the invented Traditional Chinese Medicine composition on primary hepatic carcinoma are not so obvious, PR rate is only 2.4%, however, Karnofsky scores, body weights, appetites of the primary hepatic carcinoma patients increased obviously compared with before treatment, at the same time, symptoms such as fatigue, dry mouth, thirst, cancer pain, dizziness, abdominal distension and cellular immune functions are improved to some extent compared with those of before treatment. The invented Traditional Chinese Medicine

20 composition has better clinical effects on treatment of gastric carcinoma, PR rate is 10.2%, Karnofsky scores, body weights, appetites of the gastric carcinoma patients increased obviously compared with those of before treatment, at the same time, symptoms such as fatigue, gastric discomfort, loss of appetite, dry mouth, thirst, cancer pain, dizziness, abdominal distension are ameliorated compared with before treatment.

During the course of treatment, few patients were damaged in liver, kidney functions and hematopoietic

25 systems, some patients had suspicious adverse reactions including fever, alopecie, choking, short of breath, non cancer pain, nausea and vomit. constipation and bleeding, but they still do not stop using the test composition.

Application example 2. Clinical trail summary of adjunctive therapy using the invented Traditonal

30 Chinese Medicine composition on primary hepatic carcinoma

Object and method

I choice of tested object

1. Chinese medicine syndrome ~~diagosis~~ diagnosis criterion: the same as example 1

2. Western medicine diagnosis criterion: the same as diagnosis criterion of primary hepatic carcinoma

40

mentioned in application example 1.

   3. Inclusion criterion

     (1) Patients of stage □ without taboo of intervention and ~~chemothery~~chemotherapy.

     (2) Others are the same as application example 1

5   4. Excluding case criterion

     The same as application example 1 except condition mentioned in (4)

   II . Methods of clinical trails

   1.Trail design:

   Adopting randomized controlled trial.

10   Dividing into different groups via simple and random methods, The researchers acquired random number through operating random key (INV,RAN) on Casio (fx-3600p) calculators, making into random allocated cards, sealed in the envelopes, serial number of envelope is the same as that of card, certificated. Suitable cases entered into trail, according to entering time sequence, opened the envelope and divided according to the cards properly.

15   5. ~~Adiministration~~ Administration manner and dosage:

   Treat group

   Begin to take the invented Traditional Chinese Medicine composition orally 1 week before the first hepatic artery intervention chemotherapy plus embolism therapy, twice each day, 15ml each time (1 ml containing crude drugs 0.75g), taken once in the early morning and evening, taken with warm water, 20 performing the second hepatic artery intervention chemotherapy plus embolism therapy after 4 weeks, performing twice together. The invented Traditional Chinese Medicine composition is taken for consecutive 2 months.

   Control group:

   4 weeks after first time hepatic artery intervention chemotherapy plus embolism therapy, performing 25 second hepatic artery intervention chemotherapy plus embolism, performing twice ~~togather~~together.

   6. Chemotherapy regimen:

   DDP   60mg/M^2

   ADM   40mg/M^2

   5-Fu   600mg/M^2

30   7. Embolism methods: iodized oil plus gelatin sponge

   Dosages of iodized oil and gelatin sponge should be recorded in details in clinical observation label.

   8. Course of treatment: 2 months. (the treatment course of– Stage II III patients will also be 2 months for the ~~convience~~convenience of future statistical analysis of data.)

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9. Observed items and methods:

The same as application example 1

III. Therapeutic effects assessment criterions.

1. The same as application example 1.

2. Assessments of life spans and survival rates:

life spans after treatment refer to the time from beginning of treatment to death or the last follow-up.

Follow-up need at least 1 year after treatment.

IV. Handling and summarizing of clinical trail data

Collecting all data, inputting into computers, constructing database using EPI INF06 software, making statistical treatment and analysis, summarize clinical trails, making objective assessment about clinical adjunctive therapeutic effects and safety of the invented Traditional Chinese Medicine composition on primary hepatic carcinoma.

Statistical method: enumeration data are analyzed by X^2 test, ranked data are analyzed by Wilcoxon rank sum test, two sample means are checked by t-test. Logistic regression analysis is also used to analyze enumeration data. Life span and survival rate are analyzed using life table method and Kaplan-Meier method.

Results

I . General data

183 suitable cases, 124 cases for treat group, 59 cases for control group; all are diagnosed as primary hepatic carcinoma by ~~westen~~western medicine and as symptom of stagnation of poison by Traditional Chinese Medicine. Please refer to the comparable analysis for information about sex, age and disease.

II .Comparable check of two groups

1. Sex construction comparison of two groups

Table 1 sex comparison of two groups

group	cases	male	female
treat group	124	110	14
control	59	51	8

X^2=0.195   P=0.659

Sex comparison of two groups, there is no notable significance in the difference.

2. Age block comparison of two groups

Table 2 Age block (year) comparison of two groups

42

group	cases	21-40	41-50	51-60	61-75	$\overline{x} \pm s$
treat group	124	19	40	42	23	51.2±10.0
control	59	13	19	17	10	50.1±10.6

$$X^2=1.400 \qquad\qquad t=0.650$$
$$P=0.705 \qquad\qquad P=0.516$$

Age block comparison of two groups, there is no notable significance in the difference.

3. Disease course comparison of two groups

Table 3 Disease course comparison of two groups (month)

group	cases	1-3	4-6	7-12	13-64
treat group	118	87	13	6	12
Control group	58	40	10	4	4

$$X^2=1.958 \qquad P=0.581$$

* 6 cases in treat group and 1 case in control group are not recorded.

5   Disease course comparison of two groups, there is no notable significance in the difference.

4. Past treatment comparison of two groups

Table 4 Past treatment comparison of two groups

group	cases*	untreated	operation	TCM	TAI
treat group	113	85	15	0	13
Control	58	44	8	3	3

Fisher's exact test   P=0.07

* 11 cases in treat group and 1 case in control group are not recorded.

10   Past treatment comparison of two groups, there is no notable significance in the difference.

5. Foci of Liver Cancer type comparison of two groups

Table 5   Foci of Liver Cancer type comparison of two groups

group	cases	massive type	nodular type	diffuse type
treat group	124	76	38	10
control	59	35	20	4

Fisher's exact test   P=0.879

43

Pathological diagnosis comparison of two groups, there is no notable significance in the difference.

6. Clinical stage comparison of two groups

Table 6   Clinical stage comparison of two groups

group	cases	I	II	III
treat group	124	6	92	26
control	59	1	51	7

| | | Fisher's exact test | P=0.210 |

5   Clinical stage comparison of two groups, there is no notable significance in the difference.

7. Tumor foci size comparison of two groups

Table 7 Tumor foci size * comparison of two groups

group	cases	$\overline{x} \pm s$
treat group	112	71.46±63.23
control	55	78.03±57.04

| | rank sum test | u=1.054 | P=0.292 |

*12 cases in treat group and 4 cases in control groups are massive type, not calculate size. Tumor foci
10   size is measured by product of two perpendicular maximum diameters of tumor or sum of products of

multiple foci (cm×cm) .

Tumor foci size comparison of two groups, there is no notable significance in the difference.

Table 8   Portal vein tumor embolism comparison of two groups

group	cases	negative	positive
treat group	124	104	20
control	59	46	13
		X^2=0.943	P=0.331

15   Portal vein tumor embolism comparison of two groups, there is no notable significance in the difference.

8. Karnofsky score, body weight and appetite comparison of two groups

Table 9   Karnofsky score comparison of two groups before treatment

group	cases	60-69	70-79	80-89	90-100	$\overline{x} \pm s$

treat group	124	8	56	55	5	74.7±7.0
control	59	2	22	20	15	78.4±8.4

Fisher's exact test	t=3.095
P=0.000	P=0.002

Karnofsky score comparison of two groups before treatment, there is notable significance in the difference, Karnofsky score of treat group is lower than that of control group before treatment.

Table 10　Body weight（Kg）comparison of two groups before treatment

group	cases	40-50	51-60	61-70	71-87	$\overline{x}\pm s$
treat group	123*	6	27	52	38	66.0±9.1
control	59	1	27	26	5	62.6±6.8

Fisher's exact test	t'=2.816
P=0.000	P=0.006

*Data of 1 case in treat group is lost.

5　　Body weight comparison of two groups before treatment, there is notable significance in the difference, body weight of treat group is higher than that of control group.

Table 11　Appetite (taels/day）　comparison of two groups before treatment

group	cases	2~4	4~5.9	6~7.9	8~10	$\overline{x}\pm s$
treat group	124	14	44	41	25	6.0±1.6
control	59	9	7	31	12	6.1±1.6

X^2=12.358	t=0.464
P=0.006	P=0.643

Appetite comparison of two groups before treatment, there is no notable significance in the difference.

10　9. Main symptoms and signs comparison of two groups before treatment.

Table 12　Fatigue comparison of two groups before treatment*

group	cases	Grade 0 ~~grade 0~~	Grade I ~~grade□~~	Grade II ~~grade□~~	Grade III ~~grade□~~	Grade IV ~~grade□~~
treat group	124	34	47	27	16	0
control	59	21	30	6	2	0

rank sum test	u=2.457	P=0.014

*Grade 0：none

45

Grade I : Be fatigue after activities, easy to recover

Grade II : Be fatigue after activities, difficult to recover

Grade III : be fatigue during rest

Grade IV : Lying in bed

5   Fatigue comparison of two groups before treatment, there is notable significance in the difference, fatigue level of treat group is severer than that of control ~~goup~~group.

Table 13 Dry mouth, thirst comparison of two groups before treatment[*]

group	cases	Grade 0 ~~grade 0~~	Grade I ~~grade□~~	Grade II ~~grade□~~	Grade III ~~grade□~~	Grade IV ~~grade□~~
treat group	124	98	20	6	0	0
control	59	41	15	2	1	0
			rank sum test	u=1.531	P=0.177	

*Grade 0 : none

10   Grade I : dry mouth

Grade II : dry mouth and throat, no desire for drink.

GradeIII : dry mouth and throat, desire for drink.

GradeIV : dry mouth, sore throat.

Dry mouth, thirst comparison of two groups before treatment, there is no significant difference.

15   Table 14 Bitter mouth comparison of two groups before treatment

group	cases	Grade 0 ~~grade 0~~	Grade I ~~grade□~~	Grade II ~~grade□~~	Grade III ~~grade□~~	Grade IV ~~grade□~~
treat group	124	86	28	4	6	0
control	59	50	7	2	0	0
			rank sum test	u=2.253	P=0.024	

Bitter taste of mouth comparison of two groups before treatment, there is notable significance in the difference, Bitter taste of mouth of treat group is severer than control group.

Table 15   Spontaneous perspiration comparison of two groups before treatment[*]

group	cases	Grade 0 ~~grade 0~~	Grade I ~~grade□~~	Grade II ~~grade□~~	Grade III ~~grade□~~	Grade IV ~~grade□~~
treat group	124	110	13	1	0	0
control	59	57	2	0	0	0

46

rank sum test   u=1.769   P=0.077

*Grade 0: none

Grade I: sweat occasionally after activities.

Grade II: sweat immediately after activities.

Grade III: sweat during rest

5   Grade IV: sweat vehemently.

Spontaneous perspiration comparison of two groups before treatment, there is no notable significance in

the difference.

Table 16 Night sweat comparison of two groups before treatment* ,

group	cases	Grade 0grade 0	Grade I grade☐	Grade II grade☐	Grade III grade☐	Grade IV grade☐
treat group	124	111	10	3	0	0
control	59	55	3	1	0	0

rank sum test   u=0.801   P=0.423

*Grade 0: none

10   Grade I : occasionally

Grade II : often

Grade III: every night

Grade_IV: wet cloth.

Night sweat comparison of two groups before treatment,   there is no notable significance in the

15   difference.

Table 17 Upset and tantrum comparison of two groups before treatment*

group	cases	Grade 0grade0	Grade I grade☐	Grade II grade☐	Grade III grade☐	Grade IV grade☐
treat group	124	106	9	9	0	0
control	59	52	7	0	0	0

rank sum test   u=0.643   P=0.520

*Grade 0: none

Grade I : upset, self-controllable

20   Grade II : upset, self-uncontrollable

GradeIII: burning sensation of five centres, irritable

GradeIV: manic

47

Upset and tantrum comparison of two groups before treatment, there is no notable significance in the difference.

Table 18 Dizziness comparison of two groups before treatment[*]

group	cases	Grade 0 ~~grade0~~	Grade I ~~grade~~	Grade II ~~grade~~	Grade III ~~grade~~	Grade IV ~~grade~~
treat group	124	112	7	5	0	0
control	59	51	6	2	0	0
			rank sum test	u=0.739	P=0.460	

*Grade 0: none

Grade□: dizzy occasionally

Grade□: dizzy regularly

Grade□: dizzy persistently

Grade□: need lie in bed

Dizziness comparison of two groups before treatment, there is no notable significance in the difference.

Table 19 Jaundice comparison of two groups before treatment[*]

group	cases	Grade 0 ~~grade0~~	Grade I ~~grade~~	Grade II ~~grade~~	Grade III ~~grade~~	Grade IV ~~grade~~
treat group	124	113	7	4	0	0
Control	59	54	3	2	0	0
			rank sum test	u=0.082	P=0.934	

*Grade 0: none

Grade I ~~Grade~~: albuginea oculi mildly stained yellow

Grade II ~~Grade~~: albuginea oculi and skin mildly stained yellow

Grade III ~~Grade~~: albuginea oculi and skin stained saffron yellow

Grade IV ~~Grade~~: albuginea oculi and skin stained deep yellow

Jaundice comparison of two groups before treatment, there is no notable significance in the difference.

Table 20 Cancer pain comparison of two groups before treatment[*]

group	cases	Grade 0 ~~grade0~~	Grade I ~~grade~~	Grade II ~~grade~~	Grade III ~~grade~~	Grade IV ~~grade~~
treat group	124	46	48	29	1	0
control	58	23	31	4	0	0

48

rank sum test   u=1.509   P=0.131

*Grade 0: none

Grade I ~~Grade~~: mild (discomfort, no upset)

Grade II ~~Grade~~: moderate (bearable, no upset)

Grade III~~Grade~~: ~~sereve~~severe   (positive position, demand painkiller)

5   Grade IV~~Grade~~: uncontrollable (upset, passive position, need painkiller to relieve)

Cancer pain comparison of two groups before treatment, there is no notable significance in the difference

Table 21   Abdominal distension comparison of two groups before treatment[*]

group	cases	Grade 0~~grade0~~	Grade I ~~grade~~	Grade II ~~grade~~	Grade III ~~grade~~	Grade IV ~~grade~~
treat group	124	47	57	12	8	0
control	59	32	21	3	3	0

rank sum test   u=2.052   P=0.040

*Grade 0: none

10   Grade I ~~Grade~~: abdominal distension , relieved after passage of gas by anus, no ascites.

Grade II ~~Grade~~: abdominal distension ,unrelieved after passage of gas by anus, no ascites.

Grade III~~Grade~~: obvious abdominal distension with small or moderate volume of ascites.

Grade IV~~Grade~~: obvious abdominal distension with large volume of ascites

Abdominal distension comparison of two groups before treatment, there is notable significance in the

15   difference, abdominal distension of treat group is severer than control group.

10. Ascites and abdomen circumference size comparison of two groups before treatment.

Table 22 Ascites comparison of two groups before treatment.

group	cases	without	with
treat group	124	113	11
control	59	51	8

X^2=0.944   P=0.331

Ascites comparison of two groups before treatment, there is no notable significance in the difference.

20

Table 23 Abdomen circumference size comparison of two groups before treatment

group	cases	$\bar{x} \pm s$

49

treat group	94	82.89±8.22
control	36	80.86±9.59

rank sum test u=1.272 P=0.203

*Data of 30 cases in treat group and 23 cases in control group are lost.

Abdomen circumference size comparison of two groups before treatment, there is no notable significance in the difference.

11. Tongue Picture and pulse tracings comparison of two groups before treatment

Table 24　Tongue Picture comparison of two groups before treatment

group	cases	thin and white	thin and yellow	yellow and greasy	yellow and thick
treat group	123	29	47	41	6
control	59	17	25	13	4

Fisher's exact test　　P=0.426

Tongue Picture comparison of two groups before treatment, there is no notable significance in the difference.

Table 25 Tongue texture comparison of two groups before treatment

group	cases	carmoisine	red	dark red/ purple dark/ cyanochroia	petechia/ ecchymosis
treat group	123	2	23	86	12
control	59	0	2	55	2

Fisher's exact test　　P=0.0024

Tongue texture comparison of two groups before treatment, there is notable significance in the difference.

Table 26　　Pulse tracings comparison of two groups before treatment

group	cases	even	astringent	string	smooth	week
treat group	123	4	35	69	12	3
control	59	0	15	28	11	5

Fisher's exact test　　P=0.089

Pulse tracings comparison of two groups before treatment, there is no notable significance in the difference.

12. AFP, γ-GT, and LDH level comparison of two groups before treatment

50

Table 27 AFP（ug/ml）comparison of two groups before treatment

group	cases	<30	30-399	≥400	$\overline{x}\pm s$
treat group	123	15	35	73	380.5±367.0
control	58	2	20	36	408.8±332.7

$$X^2=3.73 \qquad P=0.155$$

AFP comparison of two groups before treatment, there is no notable significance in the difference.

Table 28 γ-GT comparison of two groups before treatment

group	cases	$\overline{x}\pm s$
treat group	96	179.75±133.86
control	43	170.79±171.69

$$t=0.333 \qquad P=0.739$$

5   γ-GT comparison of two groups before treatment, there is no notable significance in the difference.

Table 29   LDH comparison of two groups before treatment

group	cases	$\overline{x}\pm s$
treat group	59	220.31±126.70
control	24	210.00±135.57

$$t=0.334 \qquad P=0.739$$

LDH comparison of two groups before treatment, there is no notable significance in the difference.

Above results of comparability check show that sex, age, disease courses ,past treatment methods,

10   tumor type, clinical stage, coated tongue and pulse tracings of two groups have no significant differences, except Karnofsky scores, body weights, fatigue, bitter taste of mouth, abdominal distension, tongue textures. Though comparison of Karnofsky scores, body weights, fatigue, bitter taste of mouth, abdominal distension, treat group are worse than those of control groups, considering these factors may influence therapeutic effects eonparisoncomparison, so Logistic regression analysis is necessary when comparing

15   therapeutic effects.

III.Therapeutic effects comparison

1.Total   therapeutic effects comparison

Table 30   Total therapeutic effects comparison

51

group	cases	CR(%)	PR(%)	SD(%)	PD(%)
treat group	124	0	19	97	8
		0%	15.3%	78.2%	6.5%
control	59	0	4	44	11
		0%	6.8%	74.6%	18.6%
		rank sum test	u=2.723	P=0.006	

Table 31   Logistic regression analysis of total therapeutic effects*

factor	coefficient	Wald	D/F	P value	RR	95% confidence interval of RR
group	1.540	8.533	1	0.003	4.66	1.66~13.11
Karnofsky scores	0.102	7.705	1	0.006	1.11	1.03~1.19
constant	-6.303	5.228	1	0.022		

* Dividing clinical therapeutic effects into two categories, that is, more than stability and progession disease variable including group, Karnofsky scores, body weight, appetite, bitter taste of mouth, abdominal distension, tongue texture, using backward method to select variables,   select results show that only group and Karnofsky scores have notable significance. Hosmer & Lemeshow test of model, $X^2=0.199,P=0.995$, indicating model fitting is good.

CR, PR, SD and PD rates of treat group are 0%,15.3%,78.2%,6.5% respectively, CR, PR, SD and PD rates of control group are 0%,6.8%,74.6% and 18.6% respectively. There is notable signicance significance in the difference between two groups.

Considering that factors including Karnofsky scores, body weight, fatigue, bitter mouth, abdominal distension may influence therapeutic effects, so Logistic regression analysis is necessary when comparing therapeutic effects. Results indicate that therapeutic effects between two groups have notable significance in their differences, relative risk (RR) of control group to treat group is 4.66, suggesting that the risk of disease progression of control group is 4.66 times of the treat group.

2. Life spans and survival rates comparison of two groups after treatment.

Table 32   Death comparasion comparison of two groups 8 weeks after treatment

group	cases	survival	death (cause)				
			hepatic coma	Hepatorrhe-xis	upper gastrointestinal bleeding	failure	others
treat group	124	102	3	6	4	7	2

52

| control | 59 | 48 | 2 | 1 | 5 | 2 | 1 |

combined death cases X^2=0.022   P=0.882

Death comparasion comparison of two groups 8 weeks after treatment, there is no notable significance in the   difference.

Talbe33   Death comparasion comparison of two groups 1.5 years after treatment

group	cases	survival	death (cause)					
			hepatic coma	Hepatorr he-xis	upper gastrointestin-al bleeding	failure	hepatorenal syndrome	others
Treat group	124	40	8	5	18	38	3	12
Control	59	21	3	4	10	11	3	7

combined death cases X^2=0.20   P=0.655

Death comparasion comparison of two groups 1.5 years after treatment, there is no notable significance
5   in the difference.

Table 34   Life span and survival rate comparison of two groups 1.5 year after treatment(-) *

group	cases	complete data	censored	% censored
Treat group	122	83	39	32.0
control	58	38	20	34.5

*Data of 2 cases in treat group and 1 case of control group are lost.

Table 35   Life span and survival rate comparison of two groups 1.5 year after treatment(二)*

group	cases	Average survival time (month)	Median survival time (month)	1 year survival rate	
		$\bar{x} \pm se$	$\bar{x} \pm se$	%	se
treat group	122	11±1	11±2	40.25	4.48
control	58	11±1	10±4	45.75	6.63

short term effect Breslow test，statistic=0.04，P=0.851

Long term effect Log-rank test，statistic =0.00，P=0.983

survival rate Comparison of two groups ,Gehan test，statistic =0.035，P=0.852

10   Life span and survival rate comparison of two groups 1.5 year after treatment: 1 year survival rate of treat group and control group are 40.25%, 45.75% respectively, there is no notable significance in the

difference. between two groups.

3. Tumor foci size comparison of two groups after treatment

Table 36   Tumor foci size comparison of two groups after treatment*

group	cases	before treatment	after treatment	difference (after-before)
		$\overline{x} \pm s$	$\overline{x} \pm s$	$\overline{x} \pm s$
treat group	112	71.5±63.2	53.8±48.4	-17.6±29.9
control	55	78.0±57.0	71.8±56.8	-6.9±23.7

* Tumor foci size is measured by product of two perpendicular maximum diameters of tumor or sum of products of multiple foci(cm×cm). 10 cases in treat group and 4 cases in control groups are diffuse type, Data of 2 cases in treat group are lost.

Comparison of treat group before and after treatment, t=6.24, P=0.000;

Comparison of control group before and after treatment, t=2.14, P=0.037;

Difference (after-before) comparison of two groups, t=2.31, P=0.022。

Tumor foci size comparison of treat group before and after treatment, there is notable significance in the difference.

Tumor foci size comparison of control group before and after treatment, there is notable significance in the difference..

Tumor foci size difference (after-before) comparison of two groups, there is notable significance in the difference.

4. Karnofsky scores comparison of two groups after treatment

Table 37 Karnofsky scores comparison of two groups after treatment

group	before treatment	after treatment	difference (after-before)
	$\overline{x} \pm s$ (n)	$\overline{x} \pm s$ (n)	$\overline{x} \pm s$ (n)
Treat group	74.7±7.0(124)	85.7±9.1(108)	11.8±7.2(108)
control	78.4±8.4(59)	77.5±11.5(55)	-0.5±8.5(55)

Comparison of treat group before and after treatment, t=16.87, P=0.000;

Comparison of control group before and after treatment, t=0.396, P=0.694;

Difference (after-before) comparison of two groups, t=9.584, P=0.000;

Karnofsky scores comparison of treat group before and after treatment, there is notable significance in the difference..

Karnofsky scores comparison of control group before and after treatment, there is no notable

54

significance in the difference..

Karnofsky scores difference (after-before) comparison of two groups, there is notable significance in the difference.

5. Body weight comparison of two groups after treatment

Table 38   Body weight (Kg) t comparison of two groups after treatment

group	before treatment	after treatment	difference (after-before)
	$\overline{x} \pm s$ (n)	$\overline{x} \pm s$ (n)	$\overline{x} \pm s$ (n)
Treat group	66.0±9.1(123)	66.5±8.5(108)	1.3±2.8(107)
Control	62.6±6.8(59)	62.2±7.2(54)	-0.5±2.4(54)

Comparison of treat group before and after treatment, t=0.04, P=0.965;

Comparison of control group before and after treatment, t=1.73, P=0.108;

Difference (after-before) comparison of two groups, t=9.584, P=0.000;

Body weight comparison of treat group before and after treatment, there is no notable significance in the difference..

Body weight comparison of control group before and after treatment, there is no notable significance in the difference.-

Body weight difference (after-before) comparison of two groups, there is notable significance in the difference..

6. Appetite comparison of two groups after treatment

Table 39 Appetite (taels/day) comparison of two groups after treatment

group	before treatment	after treatment	difference (after-before)
	$\overline{x} \pm s$ (n)	$\overline{x} \pm s$ (n)	$\overline{x} \pm s$ (n)
Treat group	6.0±1.6(124)	6.9±1.6(112)	1.1±1.7(112)
Control	6.1±1.6(59)	6.4±1.6(55)	-0.3±1.6(55)

Comparison of treat group before and after treatment, t=4.98, P=0.000;

Comparison of control group before and after treatment, t=5.92, P=0.000;

Difference (after-before) comparison of two groups, t=2.61, P=0.010。

Appetite comparison of treat group before and after treatment, there is notable significance in the difference.

Appetite comparison of control group before and after treatment, there is notable significance in the difference.

Appetite difference (after-before) comparison of two groups, there is notable significance in the difference.

7. Main clinical symptoms and signs improvement comparison of two groups after treatment

Table 40 Fatigue comparison of two groups after treatment[*]

group	cases	aggravation	no change	Improved 1 grade	Improved 2 grades	Improved 3 grades
Treat group	113	4	32	42	21	14
Control	55	3	30	18	4	0
rank sum test				u=3.98	P=0.000	

* Data of 11 cases in treat group and 4 cases of control group are lost.

Meaning of Improved grade is the same as application example 1.

Fatigue comparison of two groups after treatment, there is notable significance in the difference.

Table 42   Dry mouth and thirst improvement comparison of two groups after treatment[*]

group	cases	aggravation	no change	Improved 1 grade	Improved 2 grades	Improved 3 grades
Treat group	113	2	88	17	6	0
control	55	0	43	12	0	0
rank sum test				u=0.25	P=0.806	

* Data of 11 cases in treat group and 4 cases in control group are lost.

Meaning of Improved grade is the same as application example 1.

Mouth and thirst improvement comparison of two groups after treatment—.__There is no notable significance in the difference.

Table 43 Bitter mouth improvement comparison of two groups after treatment

group	cases	aggravation	no change	Improved 1 grade	Improved 2 grades	Improved 3 grades
Treat group	113	0	77	26	4	6
control	55	1	49	5	0	0
rank sum test				u=3.45	P=0.001	

* Data of 11 cases in treat group and 4 cases in control group are lost.

Bitter mouth improvement comparison of two groups after treatment, there is notable significance in the difference.

56

Table 44   Spontaneous perspiration improvement comparison of two groups after treatment[*]

group	cases	aggravation	no change	Improved 1 grade	Improved 2 grades	Improved 3 grades
treat group	113	1	101	11	0	0
control	55	1	52	2	0	0

rank sum test	u=1.46	P=0.143

* Data of 11 cases in treat group and 4 cases in control group are lost.

Meaning of Improved grade is the same as application example 1.

Spontaneous perspiration improvement of comparison of two groups after treatment, there is no notable

5   significance in the difference.

Table 45   Night sweat improvement comparison of two groups after treatment[*]

group	cases	aggravation	no change	Improved 1 grade	Improved 2 grades	Improved 3 grades
treat group	113	1	103	9	0	0
control	55	1	50	4	0	0

rank sum test	u=0.33	P=0.743

* Data of 11 cases in treat group and 4 cases in control group are lost.

Meaning of Improved grade is the same as application example 1.

Night sweat improvement comparison of two groups after treatment, there is no notable significance in

10   the difference.

Table 46 Upset and tantrum improvement comparison of two groups after treatment

group	cases	aggravation	no change	Improved 1 grade	Improved 2 grades	Improved 3 grades
treat group	114	0	96	9	9	0
control	54	0	48	6	0	0

rank sum test	u=0.96	P=0.339

* Data of 10 cases in treat group and 5 cases in control group are lost.

Improved 1 grade: Upset and tantrum lowered 1 grade after treatment, for example, upset and self-uncontrollable, improved to be upset and self-controllable.

15   Improved 2 grades: upset and tantrum lowered 2 grades after treatment, for example, burning sensation of five centres and tantrum, improved to be upset and self-controllable.

57

Improved 3 grades: upset and tantrum lowered 3 grades after treatment, for example, vesania, improved to be upset and self-controllable.

Upset and tantrum improvement comparison of two groups after treatment, there is no notable significance in the difference .

5

Table 47 Dizziness improvement comparison of two groups after treatment

group	cases	aggravation	no change	Improved 1 grade	Improved 2 grades	Improved 3 grades
treat group	114	1	101	8	4	0
control	54	3	48	3	0	0
			rank sum test	u=1.77	P=0.077	

* Data of 10 cases in treat group and 5 cases in control group are lost.

Meaning of Improved 1 grade and 2 grades are the same as application example 1.

Improved 3 grades means dizziness lowered 3 grades compared with before treatment, for example,

10   need lie in bed, or improve to be dizzy occasionally.

Dizziness improvement of comparison of two groups after treatment, there is no notable significance in the difference.

Table 48 Jaundice improvement comparison of two groups after treatment

group	cases	aggravation	no change	Improved 1 grade	Improved 2 grades	Improved 3 grades
treat group	114	4	103	5	2	0
control	54	5	47	1	1	0
			rank sum test	u=1.52	P=0.128	

15   * Data of 10 cases in treat group and 5 cases in control group are lost.

Improved 1 grade: Jaundice lowered 1 grade after treatment, for example, albuginea oculi and skin slightly stained yellow, improved to only albuginea oculi slightly stained yellow.

Improved 2 grades: Jaundice lowered 2 grades after treatment, for example, albuginea oculi and skin stained saffron yellow, improved to only albuginea oculi slightly stained yellow.

20   Improved 3 grades: Jaundice lowered 3 grades after treatment, for example, albuginea oculi and skin stained deep yellow or dark yellow, improved to only albuginea oculi slightly stained yellow.

Jaundice improvement comparison of two groups after treatment, there is no notable significance in the

58

difference .

Table 49 Cancer pain improvement comparison of two groups after treatment

group	cases	aggravati on	no change	Improved 1 grade	Improved 2 grades	Improved 3 grades
treat group	114	0	44	47	22	1
control	53	1	26	23	3	0

rank sum test	u=2.20	P=0.028

* Data of 10 cases in treat group and 6 cases in control group are lost.

Meaning of Improved grade is the same as application example 1.

Cancer pain improvement comparison of two groups after treatment, there is notable significance in the difference.

Table 50 Abdominal distension improvement comparison of two groups after treatment

group	cases	aggravati on	no change	Improved 1 grade	Improved 2 grades	Improved 3 grades
treat group	114	3	43	56	9	3
control	53	5	33	12	1	2

rank sum test	u=3.70	P=0.000

* Data of 10 cases in treat group and 6 cases in control group are lost.

Meaning of Improved grade is the same as application example 1.

Abdominal distension improvement comparison of two groups after treatment, there is notable significance in the difference.

8. Main symptoms and signs disappearance rates comparison of two groups after treatment

Table 51 Main symptoms and signs disappearance rates comparison of two groups after treatment

symptoms	group	total cases	original cases	disappearanc e cases	disappearan ce rate	
fatigue	treat group	113*	82	72	87.8	$X^2=6.35$ P=0.009
	control	55	35	22	62.9	
dry mouth thirst	treat group	113*	24	23	95.8	Fisher's exact test P=0.040
	control	55	15	11	73.3	

bitter mouth	treat group	113*	37	36	97.3	Fisher's exact test P=0.103
	control	55	7	4	57.1	
spontaneous perspiration	treat group	113*	11	11	100.0	
	control	55	2	2	100.0	
night sweat	treat group	113*	10	9	90.0	Fisher's exact test P=0.549
	control	55	4	3	75.0	
upset and tantrum	treat group	114#	18	18	100.0	
	control	54	6	6	100.0	
dizziness	treat group	114#	12	11	91.7	Fisher's exact test P=0.037
	control	54	7	3	42.9	
jaundice	treat group	114#	10	7	70.0	Fisher's exact test P=0.657
	control	54	3	1	33.3	
cancer pain	treat group	114+	72	66	91.7	Fisher's exact test P=0.199
	control	53	32	26	81.3	
abdominal distension	treat group	114+	70	66	94.3	Fisher's exact test P=0.001
	control	53	25	14	56.0	

* Data of 11 cases in treat group and 4 cases in control group are lost.

Data of 10 cases in treat group and 5 cases in control group are lost.

+ Data of 10 cases in treat group and 6 cases in control group are lost.

Disappearance rates comparison of fatigue, dry mouth, thirst, dizziness, abdominal distension of two groups after treatment, there is notable significance in the difference. Disappearance rates comparison of bitter mouth spontaneous perspiration, night sweat, upset, tantrum, jaundice, cancer pain of two groups after treatment,there is no notable significance in the difference .

9. WBC counting comparison of two groups after treatment

Table 52 WBC counting comparison of two groups after treatment*

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group	cases	aggravati on	no change	Improved 1 grade	Improved 2 grades	Improved 3 grades
treat group	114	6	91	8	8	1
control	54	5	44	5	0	0
	rank sum test		u=1.45	P=0.148		

● Grade WBC accurately according to "WHOgrade criterions for acute and subacute toxicity reactions of the anti-cancer drugs", see details in application example 1.

WBC counting comparison of two groups after treatment, there is no notable significance in the difference .

5   10. Granulocytes counting comparison of two groups after treatment

Table53 Granulocytes counting comparison of two groups after treatment*

group	cases	aggravati on	no change	Improved 1 grade	Improved 2 grades	Improved 3 grades
treat group	117	2	103	6	6	0
control	59	5	51	1	1	1
	rank sum test		u=2.07	P=0.039		

* Grade granulocytes accurately according to "WHOgrade criterions for acute and subacute toxicity reactions of the anti-cancer   drugs", see details in application example 1.

Granulocytes counting comparison of two groups after treatment, there is notable significance in the

10   difference.

11. Hemoglobin comparison of two groups after treatment

Table 54 Hemaglobin comparison of two groups after treatment*

group	cases	aggravati on	no change	Improved 1 grade	Improved 2 grades	Improved 3 grades
treat group	118	16	91	10	1	0
control	59	11	40	6	0	2
	rank sum test		u=0.16	P=0.870		

* Grade hemoglobin accurately according to WHO"grade criterions for acute and subacute toxicity reactions of the anti-cancer drugs", see details in application example 1.

15   Hemoglobin comparison of two groups after treatment, there is no notable significance in the difference.

12. Platelets counting comparison of two groups after treatment

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Table 55 Platelets counting comparison of two groups after treatment[*]

group	cases	aggravation	no change	Improved 1 grade	Improved 2 grades	Improved 3 grades
treat group	117	12	83	12	8	2
control	59	7	47	4	1	0

rank sum test	u=1.48	P=0.139

- Grade platelets accurately according to "WHOgrade criterions for acute and subacute toxicity reactions of the anti-cancer drugs", see details in application example 1.

- Phatelets counting comparison of two groups after treatment, there is no notable significance in the difference .

13 .Immune function comparison of two groups after treatment

Table 56 CD3 comparison of two groups before and after treatment

group	cases	Before treatment	8 weeks after treatment	difference(after-before)
		$\overline{x} \pm s$	$\overline{x} \pm s$	$\overline{x} \pm s$
treat group	58	46.6±21.0	50.8±21.5	4.3±8.0
control	22	58.9±7.0	55.5±7.6	-3.4±8.2

Comparison of treat group before and after treatment, t=4.06, P=0.000;

Comparison of control group before and after treatment, t=1.95, P=0.065;

Difference (after-before) comparison of two groups, t=3.80, P=0.000.

CD3 comparison of treat group before and after treatment, there is notable significance in the difference.

CD3 comparison of control group before and after treatment, there is no notable significance in the difference.

CD3 (after-before) comparison of two groups, there is notable significance in the difference.

Table 57 CD4 comparison of two groups before and after treatment

group	cases	Before treatment	8 weeks after treatment	difference (after-before)
		$\overline{x} \pm s$	$\overline{x} \pm s$	$\overline{x} \pm s$

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treat group	58	31.4±14.2	36.0±15.4	4.6±5.1
control	22	39.4±7.4	40.8±7.6	1.4±7.8

Comparison of treat group before and after treatment, t=6.90, P=0.000;

Comparison of control group before and after treatment, t=0.83, P=0.416;

Difference (after-before) comparison of two groups, t'=1.81, P=0.080.

CD4 comparison of treat group before and after treatment, there is notable significance in the difference

CD4 comparison of control group before and after treatment, there is no notable significance in the difference.

CD4 difference (after-before) comparison of two groups, there is no notable significance in the difference.

Table 58 CD8 comparison of two groups before and after treatment

group	cases	Before treatment	8 weeks after treatment	difference (after-before)
		$\overline{x} \pm s$	$\overline{x} \pm s$	$\overline{x} \pm s$
treat group	58	28.0±12.7	27.7±12.2	-0.4±3.6
control	22	36.3±7.8	35.2±9.1	-1.0±6.0

Comparison of treat group before and after treatment, t=0.83, P=0.412;

Comparison of control group before and after treatment, t=0.82, P=0.422;

Difference (after-before) comparison of two groups, t'=0.49, P=0.632.

CD8 comparison of treat group before and after treatment, there is no notable significance in the difference.

CD8 comparison of control group before and after treatment, there is no notable significance in the difference.

CD8 (after-before) comparison of two groups, there is no notable significance in the difference .

Table 59 CD4/CD8 comparison of two groups before and after treatment

group	cases	Before treatment	8 weeks after treatment	difference(after-before)
		$\overline{x} \pm s$	$\overline{x} \pm s$	$\overline{x} \pm s$
treat group	56	1.12±0.28	1.32±0.22	0.19±0.18

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| control | 21 | 1.11±0.23 | 1.23±0.19 | 0.11±0.13 |

Comparison of treat group before and after treatment, t=7.96, P=0.000;

Comparison of control group before and after treatment, t=3.89, P=0.022;

Difference (after-before) comparison of two groups, t=1.77, P=0.080.

CD4/CD8 comparison of treat group before and after treatment, there is notable significance in the

5   difference.

CD4/CD8 comparison of control group before and after treatment, there is notable significance in the

difference.

CD4/CD8 difference (after-before) comparison of two groups ,there is no notable significance in the

difference.

10

Table 60 NK cell comparison of two groups before and after treatment

group	cases	Before treatment	8 weeks after treatment	difference(after-before)
		$\overline{x}\pm s$	$\overline{x}\pm s$	$\overline{x}\pm s$
treat group	30	32.6±15.1	39.7±14.8	7.1±10.2
control	9	49.4±13.1	39.3±9.5	-10.1±10.7

Comparison of treat group before and after treatment, t=3.83, P=0.001;

Comparison of control group before and after treatment, t=2.84, P=0.022;

Difference (after-before) comparison of two groups, t=4.40, P=0.000.

15   NK cell comparison of treat group before and after treatment, there is notable significance in the

difference.

NK cell comparison of control group before and after treatment, there is notable significance in the

difference.

NK cell difference (after-before) comparison of two groups, there is notable significance in the

20   difference.

14. γ -GT comparison of two groups after treatment

Table 61 γ -GT comparison of two groups after treatment

group	Before treatment	8 weeks after treatment	difference (after-before)
	$\overline{x}\pm s$ (n)	$\overline{x}\pm s$ (n)	$\overline{x}\pm s$ (n)

| treat group | 179.75±133.86(96) | 148.75±111.50(96) | -31.00±112.02(96) |
| control | 170.79±171.69(43) | 164.37±138.24(41) | -8.58±170.05(41) |

Comparison of treat group before and after treatment, t=2.711, P=0.008;

Comparison of control group before and after treatment, t=0.323, P=0.748;

Difference（after-before）comparison of two groups, t=0.911, P=0.364.

γ-GT comparison of treat group before and after treatment ,there is notable significance in the difference.

γ-GT comparison of control group before and after treatment, there is no notable significance in the difference.

γ-GT difference（after-before）comparison of two groups, there is no notable significance in the difference.

15. LDH comparison of two groups after treatment

Table 62 LDH comparison of two groups after treatment

| group | Before treatment | 8 weeks after treatment | difference（after-before） |
	$\overline{x}\pm s$（n）	$\overline{x}\pm s$（n）	$\overline{x}\pm s$（n）
treat group	220.31±126.70(59)	190.05±128.29(58)	-45.54±98.30(57)
control	210.00±135.57(24)	194.09±130.45(23)	-19.39±84.72(23)

Comparison of treat group before and after treatment, t=3.498, P=0.001;

Comparison of control group before and after treatment, t=1.098, P=0.284;

Difference（after-before）comparison of two groups, t=1.118, P=0.267.

LDH comparison of treat group before and after treatment, there is notable significance in the difference.

LDH comparison of control group before and after treatment, there is no notable significance in the difference

LDH difference（after-before）comparison of two groups, there is no notable significance in the differencee

四.Results of imageology examinations after treatment

1.B type ultrasonic examination：

116 cases in treat group and 55 cases in control group are rechecked by B type ultrasonic examination

after treatment.

2. CT and MRI examination:

83 cases in treat group and 33 cases in control group are rechecked by CT..

18 patients in treat group and 7 patients in control group are rechecked by MRI.

5   五. Safety assessment

All safety indexes are normal before treatment, the abnormal cases after treatment are recorded in following table.

Doubtful adverse reaction	treat group		control group		RR	P value
	positive cases/total cases	incidence rate	positive cases/total cases	incidence rate		
Hemoglobin reduction	16/124	12.9%	8/59	13.6%	0.95	0.902
RBC reduction	0/121	0.0%	0/59	0.0%	.	
WBC reduction	6/120	5.0%	5/55	9.1%	0.55	0.325
Granulocyte reduction	1/119	0.8%	4/59	6.8%	0.12	0.042
Platelet reduction	12/124	9.7%	5/59	8.5%	1.14	0.793
Bilirubin increase	4/112	3.6%	7/53	13.2%	0.27	0.039
AKP rising	0/123	0.0%	2/58	3.4%	.	
GPT rising	7/116	6.0%	2/58	3.4%	1.75	0.720
BUN rising	0/119	0.0%	0/54	0.0%	.	
serum creatinine rising	2/123	1.6%	0/59	0.0%	.	
Abnormal urine protein	0/123	0.0%	0/59	0.0%	.	
~~Abnormal~~ Abnormal urine RBC	0/120	0.0%	0/59	0.0%	.	
fecal occult blood	1/120	0.8%	0/59	0.0%	.	

10   Safety study results of two groups after treatment demonstrate that incidence rates of granulocyte reduction, BUN rising of treat group is lower than those of control group (P<0.05). Iincidence rates, RR of

other items of two groups and statistical analysis results, there is no notable significance in the difference. See details in above table.

六. Adverse event observations

Results of adverse event observations of two groups after treatment are shown in ~~followint~~ following

5   table:

doubtful adverse events	treat group （n=124）		control group （n=59）		RR	P value
	positive cases*	incidence rate	positive cases**	incidence rate		
fever	57	45.9%	26	44.1%	1.04	0.810
alopecie	21	16.9%	14	23.7%	0.71	0.275
oral cavity ulcer	0	0.0%	1	1.7%	.	
cutaneous reaction	0	0.0%	1	1.7%	.	
choking and short of breath	1	0.8%	8	13.6%	0.06	0.000
non cancer pain	31	25.0%	16	27.1%	0.92	0.759
hypersensitiveness	1	0.8%	0	0.0%	.	
nausea and vomit	49	39.5%	34	57.6%	0.67	0.021
constipation	2	1.6%	8	13.6%	0.12	0.002
bleeding	0	0.0%	1	1.7%	.	

*positive cases: if one patient had one symptom, recorded as one case, if one patient had two symptoms, recorded as two cases.

During the courses of treatment, some patients in both groups had adverse effects including alopecie, oral cavity ulcer etc, incidence rate and RR of each symptom, statistical analysis results are shown in above

10   table.

During the courses of treatment, incidence rates comparison of choking, short of breath, cancer pain, nausea and vomit, constipation of two groups, there is notable significance in the difference. Judging from incidence rate and RR, the treat group is lower than those of control group. other symptoms comparison of two groups, there is no notable significance in the difference.

15   There are 90 cases in treat group who had at least one doubtful adverse reaction, total incidence of doubtful adverse reaction is 72.6% （90/124）, there are 53 cases in control group who had at least one doubtful adverse reaction, total incidence of doubtful adverse reaction is 89.8% （53/59）, the relative risk (RR) of doubtful adverse reaction of treat group is 0.808 (95% confidence interval: 0.704~0.928), indicating the risk of doubtful adverse reaction of treat group is lower than that of control group.

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Conclusions

183 eligible patients entered into the clinical trails, of which 124 cases for treat group, 59 cases for control group, all were diagnosed as primary hepatic carcinoma by ~~westen~~western medicine, and as symptom of stagnation of poison by ~~Traditioanl~~ Traditional Chinese Medicine.

5   Results of comparability test before treatment show that the comparison of Karnofsky scores, body weights, fatigue, bitter mouth, abdominal distension, tongue textures of two groups before treatment, there is notable significance in the difference. But the comparison of sex, age, disease courses ,past treatment methods, tumor type, clinical stage, coated tongue and pulse tracings of two groups, there is no notable significance in the difference. Though comparison of Karnofsky scores, body weights, fatigue, bitter

10   mouth, abdominal distension, treat group are worse than those of control groups, considering that these factors may influence therapeutic effects, so we performed logistic regression analysis when comparing therapeutic effects in the research, to determine the influences of these factors on therapeutic effects comparison of two groups.

15   CR, PR, SD and PD rates of treat group are 0%, 15.3%, 78.2%, 6.5% respectively, CR, PR, SD and PD rates of control group are 0%, 6.8%, 74.6% and 18.6% respectively. After ~~comparsion~~ comparison of two groups, there is notable significance in the difference.

Considering that such factors as Karnofsky scores, body weight, fatigue, bitter mouth, abdominal ~~distension~~ distention ~~the~~ may influence therapeutic effects, so we performed logistic regression analysis

20   when comparing therapeutic effects, introducing the above variables to the model and choosing them by retreating method-. Selected Results indicate that there is notable significance in difference of group and Karnofsky scores. There is notable significance in the difference of therapeutic effects of groups. Relative risk scale (RR) of control group to treat group is 4.66, suggesting that the risk of disease progression of control group is 4.6 times of treat group.

25   Above results indicate that the invented Traditional Chinese Medicine composition, serving as adjunctive therapy on intervention chemotherapy and embolism treatment of primary hepatic carcinoma, has better clinical therapeutic effects , exerting certain synergistic functions.

After 1.5 years of follow-up, 1 year survival rate of treat group and control group are 40.3% ,45.8% respectively, results of survival analysis show that both short term effect (Breslow test) and long term

30   effect(Log-rank test) of two groups, there is no notable significance in the difference of survial time. Indicating that the invented Traditional Chinese Medicine composition adjunctive therapy on primary hepatic carcinoma patients who received intervention and embolism treatments failed to elongate the survival time, compared with treatment of solely intervention and embolism.

Results of solid ~~tomor~~ tumor foci size assessment show:

Tumor foci size difference (after-before) comparison of two groups shows that there is notable significance in the difference, minimized extent of the tumor foci size of treat group is greater than that of control group. Tumor foci size comparison of treat group before and after treatment shows that there is notable significance in the difference, tumor minimized obviously after treatment compared with before treatment; Tumor foci size comparison of control group before and after treatment ~~aslo~~ also shows that there is notable significance in the difference, tumor minimized obviously after treatment compared with before treatment. Suggesting that the invented Traditional Chinese Medicine composition, serving as adjunctive therapy on intervention chemotherapy and embolism treatment of primary hepatic carcinoma patients, can minimize tumor foci obviously, which outweighs therapeutic effects of the group received sole intervention chemotherapy and embolism treatment.

Results of main symptoms improvement show:

Karnofsky score of treat group increased obviously after treatment compared with that of before treatment, and the Karnofsky score increase extent of treat group is greater than control group, Karnofsky score of control group has no obvious increase after treatment compared with that of before treatment; Fatigue of patients in both groups improved obviously after treatment, fatigue improvement extent and fatigue disappearance rate of treat group is greater than that of control group.

Appetite of patients in both groups increased obviously after treatment, symptoms including dry mouth, thirst, bitter taste of mouth, spontaneous perspiration, night sweat, upset, tantrum, dizziness, jaundice, cancer pain, abdominal distension are all improved or have high disappearance rates, for improvement extent of bitter mouth, cancer pain and dizziness, treat group is higher than that of control group; for disappearance rates of dry mouth, thirst, dizziness, abdominal distension, treat group is higher than those of control group, other symptoms comparison in improvement extent and disappearance rate of two groups shows that there is no notable significance in the differences.

Above results indicate that the invented Traditional Chinese Medicine composition, serving as adjunctive therapy on intervention chemotherapy and embolism treatment of primary hepatic carcinoma patients, can ameliorate patients survival qualities, improve clinical symptoms, has better adjunctive ~~therapeutical~~ therapeutic effects.

Laboratory examination results demonstrate:

CD3、CD4 , CD4/CD8 and NK cells of treat group increased obviously after treatment compared with those of before treatment ($P<0.05$),furthermore, the CD3 and NK cell difference (after-before) of treat group are higher than those of control group （ $P<0.05$） , while changes of CD3、CD4 , CD4/CD8 and NK cells of

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control group are not so obvious before treatment, NK cells of control group reduced obviously after treatment compared with   that of before treatment.

Above results indicate that the invented Traditional Chinese Medicine composition, serving as adjunctive therapy on intervention chemotherapy and embolism treatment of primary hepatic carcinoma patients, has certain functions of stimulating immune responses, can assist intervention chemotherapy and embolism treatment to inhibit cancer cells.

Results of this randomized controlled trial demonstrate that the invented Traditional Chinese Medicine composition, serving as adjunctive therapy on intervention chemotherapy and embolism treatment of primary hepatic carcinoma patients, has better clinical therapeutic effects, can exert synergistic functions, can ameliorate patients survival qualities, improve clinical symptoms of patients and enhance cellular immune function of patients, can be used as adjunctive therapy on intervention chemotherapy and embolism treatment of patients primary hepatic carcinoma (considered as ~~sympton~~ symptom of stagnation of poison by ~~Traditinal~~ Traditional Chinese Medicine), clinical application is quite safe.

Application example 3 Clinical trail summary of adjunctive therapy using the invented ~~Traditonal~~ Traditional Chinese Medicine composition on gastric carcinoma

Object and method

~~Chosing~~ Choosing of eligible tested object

1. Chinese medicine syndrome ~~diagosis~~ diagnosis criterion: the same as application example 1

2.Western medicine ~~diagosis~~ diagnosis criterion: same as ~~diagosis~~ diagnosis criterion of gastric carcinoma and stage criterion mentioned in application example 1.

3. Inclusion criterion

☐   Voluntary patients.

☐   Stage☐, ☐, ☐ of gastric carcinoma patients unsuitable for surgical operation or reluctant to operation.

☐ Operations researcher of gastric carcinoma.

(4) Relapse patients of gastric carcinoma after operation unsuitable for surgical operation or reluctant to operation.

(5) Those patients who have received anti-cancer therapy, need stop therapy for more than 2 months.

☐ Age>18 years

☐ Predicted life span>3 months, survival quality Karnofsky score≥50

70

4. ~~Exclusing~~ Exclusion criterion

(1)   Patients with esophageal stenosis, cardia of stomach obstruction, pyloric obstruction, polypi, tumor, bowel obstruction; structural diseases of liver, cholecyst, pancreas, colon; gastric carcinoma like "linitis plastica" patients can not receive medication via po.

5   (2)   Others are the same as□、 □、 □~□ of application example 1.

Methods of clinical trails

1. Trail design: The same as application example 2.

2. ~~Adiministration~~ Administration manner and dosage:

Treat group

10   Taking the invented Traditional Chinese Medicine composition orally at the right time of beginning chemotherapy, twice each day, 15ml each time (1 ml containing crude drugs 0.75g), taken in the early morning and evening, taken with warm water. The invented Traditional Chinese Medicine composition is taken for consecutive 2 months.

Control group: sole chemotherapy of gastric carcinoma

15   3. Chemotherapy regimen: MF regimen

5-Fu $500mg/M^2$, V.D., d1-5

MMC $8mg/M^2$, i.v., d1

28 days ×2

4. Course of treatment: 2 months, observing for 1 month after treatment.

20   5. Observed items and methods:

(1) safety detection: The same as application example 1

(2) Therapeutic effects assessment:

① Tumor foci: Performing B type ultrasonic, X-Ray barium meal examination, air-barium double contrast examination, gastroscope, CT examination before and after treatment.

25

a.   Measurement of tumor size: multiply the two perpendicular maximum diameter.

b.   Multiple tumor foci are measured with sum of all products of multiplication (refer to products of two perpendicular maximum diameter).

c.   Diffused nodular tumor, explaining particularly.

30   □ Clinical symptom observations:

a. Main symptoms of gastric carcinoma

Lump, abdominal pain, anorexia, hemafecia, nausea, vomit, fatigue, emaciation, ascites, swollen, jaundice etc.

b. Main symptoms of stagnation of poison:

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gastric discomfort, hard lump, pain ,fatigue, progressing emaciation, vomit, haematemesis, hemafecia, dark red, purple or cyanochroia texture of tongue, white or yellow coated tongue, weak , astringent or deep pulse.

c. Karnofsky grade

☐ Laboratory examinations:

a X-Ray barium meal examination, air-barium double contrast examination （obligatory）

b Gastroscope （obligatory）

c fecal occult blood （obligatory）

d CEA （part）

e B type ultrasonic （obligatory）

f CT(done when need)

g Immunologic test: CD3, CD4, CD8, NKcell etc.

Observing methods:

Observing and recording symptoms, picture of the tongue and pulse tracings once every 2 days, observing and recording Karnofsky score and body weight once every week, blood routine test is checked at the time of beginning visit, every week after treatment; urine routine test, faeces routine test, fecal occult blood test, liver function and kidney function are checked at the time of beginning visit, every two weeks after treatment; Immunology index, ECG, heart function are checked at the time of beginning visit, every four weeks after treatment; X-Ray barium meal examination, air-barium double contrast examination, gastroscope, B type ultrasonic, CEA, bleeding time and clotting time are checked at least once at the time of beginning visit and after treatment, performing examination at any time when needed

Follow-up once every 1-2 months after treatment, Follow-up lasts at least 1 year

Therapeutic efficacy assessment criterions

1. Therapeutic efficacy assessment criterions of the tumor foci:

(1) Complete Remission (CR): tumor disappeared.

(2) Partial Remission (PR): products of two maximum diameters minimized more than 50%.

(3) Stable disease (SD): products of two maximum diameters minimized less than 50%, increased no more than 25%.

(4) Progression disease (PD): products of two maximum diameters increased more than 25%.

Total remission rate=CR+PR

2. Assessments of life spans and survival rates:

Life spans after treatment refer to the time from beginning of treatment to death or the last follow-up.

Follow-up   at least 1 year after treatment.

3. the The change of health condition: make a comparison before and after treatment, according to Karnofsky score criterions.   As for Karnofsky score criterions ,see details in application example 1.

Handling and summarizing of clinical trail data

Collecting all data, inputting medical histroy history into computers, constructing database using EPI INF06 software, making statistical treatment and analysis, writing summary of clinical trails, making objective assessment about clinical adjunctive therapeutic effects and safety of the invented Traditional Chinese Medicine composition on gastric carcinoma.

Statistical method: enumeration data are analysed analyzed by X^2 test, ranked data are analysed analyzed by Wilcoxon rank sum test, two sample means are checked by t-test. Life span and survival rate are analysed analyzed using life table method and Kaplan-Meier method.

<div align="center">Results</div>

General data

129 suitable cases, 87 cases in treat group, 42 cases in control group; all are diagnosed as gastric carcinoma by westen western medicine and as symptom of stagnation of poison by Traditonal Traditional Chinese medicine.   15 outpatient cases, 114 inpatient cases.

Comparability analysis of two groups

1. Sex comparison of two groups

Table 1 sex comparison of two groups

group	cases	male	female
treat group	87	61	26
control	42	26	16

<div align="center">X^2=0.87   P=0.35</div>

Sex comparison of two groups, there is no notable significance in the difference.

2. Age (year) comparison of two groups

Table 2 Age (year) comparison of two groups

group	cases	18-29	30-49	50-65	66-70	$\overline{x} \pm s$
treat group	87	0	14	65	8	56.2±8.0
control	42	1	8	29	4	54.6±10.8

<div align="center">Fisher's exact test   t=0.95</div>
<div align="center">P=0.566   P=0.35</div>

Age (year) comparison of two groups, there is no notable significance in the difference.

<div align="center">73</div>

3. Disease courses comparison of two groups

Table 3   Disease courses (month) comparison of two groups

group	cases	≤3	4-6	7-12	13-24	>24
treat group	87	43	19	12	7	6
control	42	24	7	6	4	1

Fisher's exact test   P=0.803

Disease courses comparison of two groups, there is no notable significance in the difference.

4. Past treatment comparison of two groups

Table 4 Past treatment comparison of two groups *

group	cases	untreated	operation	radiotherapy	chemotherapy	TCM	others
treat group	85	56	17	1	2	1	8
control	42	24	10	0	1	3	4

Fisher's exact test   P=0.517

* 2 cases in treat group are not recorded; "others" refer to combined therapy (including 1 case received intervention chemotherapy)

.Past treatment comparison of two groups, there is no notable significance in the difference.

5. Past treatment effects comparison of two groups

Table 5   Past treatment effects comparison of two groups*

group	cases	effective	ineffective	relapse
treat group	85	8	60	17
control	42	2	33	7

X^2=1.18   P=0.55

* 2 cases in treat group are not recorded.

Past treatment effects comparison of two groups , there is no notable significance in the difference.

6. Gastric carcinoma pathologic diagnosis comparison of two groups

Table 6 Gastric carcinoma pathologic diagnosis comparison of two groups

group	cases	adencarcinoma	undifferentiated carcinoma
treat group	87	86	1
control	42	38	4

Fisher's exact test   P=0.038

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Gastric carcinoma pathologic diagnosis comparison of two groups ,there is notable significance in the difference.

7.Gastric carcinoma clinical stage comparison of two groups

Table 7 Clinical stage comparison of two groups

group	cases	stage II	stage III	stage IV
treat group	87	2	16	69
control	42	1	13	28

<div align="center">Fisher's exact test   P=0.278</div>

5   Clinical stage comparison of two groups, there is no notable significance in the difference.

8.Tumor foci size comparison of two groups before treatment

Table 8 Tumor foci size comparison of two groups before treatment [*]

group	cases	$\overline{x} \pm s$
treat group	83 [**]	27.10±22.29
control	40 [**]	26.48±48.58

<div align="center">t=0.097   P=0.92</div>

*Tumor foci size is measured by product of two perpendicular maximum diameters of tumor or sum of products of multiple foci（cm×cm）.

10   ** 4 cases in treat group and 2 cases in control groups tumor foci size can not be measured:

Treat group: 1 gastric carcinomar case widely metastasized in abdominal cavity, 1 case is pathologically diagnosed as "cancer cells in ulcerative necrosis tissue", 1 case is diagnosed as" diffused, ulcerative, infiltrating carcinoma of gastric body and sinus ventriculi", 1 case is diagnosed as "poorly differentiated adenocarcinoma of cardia of stomach, with metastasis of middle and inferior

15   esophagus ".

Control group: 1 case with wide bone metastasis, 1 case is diagnosed as" diffused, ulcerative, infiltrating carcinoma of gastric body and sinus ventriculi"

Tumor foci size comparison of two groups before treatment, there is no notable significance in the difference.

20   Table 9 Tumor foci location comparison of two groups before treatment*

group	cases	cardia of stomach	gastric body	sinus ventriculi	Gastrojejunal	others
treat group	87	24	28	13	1	21
control	42	6	12	5	1	18

Fisher's exact test   P=0.197

*others: two or more than two tumor foci locations, metastasized to other locations after Gastric operation

Tumor foci location comparison of two groups before treatment, there is no notable significance in the difference.

Table 10 Metastasis comparison of two groups before treatment

group	cases	metastasis	no metastasis
treat group	87	25	62
control	42	15	27
		X^2=0.64	P=0.42

5   Metastasis comparison of two groups before treatment , there is no notable significance in the difference

Table 11 Numbers of tumor foci comparison of two groups before treatment

group	cases	1 个	2 个	>2 个
treat group	87	74	4	9
control	41	34	6	1
	Fisher's exact test		P=0.061	

Numbers of tumor foci comparison of two groups before treatment,there is no notable significance in the difference.

10   9. Karnofsky score comparison of two groups before treatment

Table 12 Karnofsky score comparison of two groups before treatment

group	cases	50-59	60-69	70-79	80-89	$\bar{x}\pm s$
treat group	87	6	34	29	18	66.78±8.83
control	42	1	15	15	11	69.04±9.32
rank sum test	u=1.045					t=1.34
	P=0.296					P=0.18

Karnofsky score comparison of two groups before treatment, there is no notable significance in the difference.

10. Body weight comparison of two groups before treatment

15   Table 13 Body weight （Kg） comparison of two groups before treatment

group	cases	35-39	40-49	50-59	60-69	>70	$\bar{x}\pm s$
treat group	87	2	12	40	26	7	57.21±9.01

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control	42	1	6	17	15	3	57.31±8.48
rank sum test		u=0.298					t=0.06
		P=0.766					P=0.95

Body weight comparison of two groups before treatment, there is no notable significance in the difference.

11. Appetite comparison of two groups before treatment

Table 14 Appetite comparison of two groups before treatment

group	cases	<4	4-5.9	6-7.9	>7.9	$\overline{x} \pm s$
treat group	87	7	37	33	10	5.46±2.02
control	42	2	13	23	4	5.81±1.29
rank sum test		u=1.253				t=1.026
		P=0.210				P=0.307

5 Appetite comparison of two groups before treatment, there is no notable significance in the difference.

12. Clinical symptoms and signs comparison of two groups before treatment

Table 15   Clinical symptoms comparison of two groups before treatment

symptoms	group	cases	Grade 0grade 0	Grade I grade I	Grade II grade II	Grade III grade III	Grade IV grade IV	u	P
gastric pain	treat group	87	10	12	32	27	6	0.88	0.38
	control	42	3	11	16	9	3		
anorexia	treat group	87	14	21	24	24	4	1.22	0.22
	control	42	5	14	18	4	1		
fatigue	treat group	87	13	17	37	16	4	1.25	0.08
	control	42	9	12	15	6	0		
dry mouth thirst	treat group	87	53	21	13	0	0	0.97	0.33
	control	42	29	9	4	0	0		
bitter taste of mouth	treat group	87	53	24	8	2	0	1.64	0.10

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symptom	group	cases						t	P
	control	42	31	10	1	0	0		
spontaneous perspiration	treat group	87	55	14	13	5	0	1.06	0.29
	control	42	30	6	6	0	0		
night sweat	treat group	87	57	16	11	3	0	1.71	0.088
	control	42	33	7	2	0	0		
upset and tantrum	treat group	87	58	17	10	2	0	1.46	0.15
	control	42	32	10	0	0	0		
dizziness	treat group	87	65	19	2	1	0	0.49	0.62
	control	42	33	8	1	0	0		
cancer pain	treat group	87	14	18	35	17	3	3.25	0.001
	control	42	13	13	15	1	0		
nausea and vomit	treat group	87	49	17	18	2	1	0.66	0.51
	control	42	26	9	4	3	0		
abdominal distension	treat group	87	32	20	28	7	0	0.25	0.80
	control	42	17	10	10	2	3		

Cancer pain extent of treat group is higher than control group before treatment. other symptoms comparison of two groups before treatment ,there is no notable significance in the difference.

Table 16 Abdominal lump size （cm×cm） comparison of two groups before treatment

group	cases	$\overline{x} \pm s$
treat group	20	51.95±40.48
control	12	61.08±82.77
t=0.419		P=0.678

Abdominal lump size （cm×cm） comparison of two groups before treatment, there is no notable significance in the difference..

Table 17 Abdominal lump texture comparison of two groups before treatment

group	cases	hard	tenacious	soft

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treat group	20	12	6	2
control	12	9	3	0
rank sum test	u=0.98	P=0.33		

Abdominal lump texture comparison of two groups before treatment, there is no notable significance in the difference.

Table 18   Abdominal lump tenderness comparison of two groups before treatment

group	cases	no tenderness	tenderness
treat group	20	2	18
control	12	4	8
Fisher's exact test	P=0.165		

5   Abdominal lump tenderness comparison of two groups before treatment, there is no notable significance in the difference.

13. Tongue demonstration comparison of two groups before treatment

Table 19   Tongue demonstration comparison of two groups before treatment

group	cases	thin and white	thin and yellow	yellow and greasy	yellow and thick	others
treat group	87	9	34	29	14	1
control	42	3	11	19	9	0
	Fisher's exact test	P=0.469				

10   Tongue demonstration comparison of two groups before treatment, there is no notable significance in the difference.

Table 20 Tongue texture comparison of two groups before treatment

group	cases	carmoisine	red	dark red	purple black	cyanochroia	petechia, ecchymosis
treat group	87	0	5	43	29	7	3
control	42	2	6	14	13	4	3
	Fisher's exact test	P=0.099					

Tongue texture comparison of two groups before treatment, there is no notable significance in the difference.

15   14. Pulse tracings comparison of two groups before treatment

Table 21 Pulse tracings comparison of two groups before treatment

group	cases	even	astringent	string	smooth	deep	weak
treat group	87	0	25	8	6	19	29
control	42	1	16	6	7	4	8

Fisher's exact test   P=0.048

Pulse tracings comparison of two groups before treatment, there is notable significance in the difference.

15. Hematology examinations of two groups

85 cases in treat group received WBC counting before treatment, 80 cases are normal, 3 cases WBC within $3.0\text{-}3.9\times10^9$/L, 2 cases WBC>10.0×10^9/L.

41 cases in control group received WBC counting before treatment, 35 cases are normal, 4 cases WBC within $3.0\text{-}3.9\times10^9$/L, 2 cases WBC>10.0×10^9/L.

42 cases in treat group received granulocyte counting before treatment, 41 cases are normal, 1 case granulocyte<2.0×10^9/L

25 cases in control group received granulocyte counting before treatment, 23 cases are normal, 2 cases granulocyte<2.0×10^9/L.

85 cases in treat group received hemoglobin test before treatment, 1 case<60g/L, 5 cases within 60-79g/L, 31 cases within 80-109g/L, 48 cases≥110g/L.

42 cases in control group received hemoglobin test before treatment, 4 cases within 60-79g/L, 18 cases within 80-109g/L, 20 cases≥110g/L.

84 cases in treat group received platelet counting before treatment, 81 cases are normal, 3 case platelets <10.0×10^9/L.

42 cases in control group received platelet counting before treatment, 38 cases are normal, 4 case platelets <10.0×10^9/L.

16. Imageology examinations of two groups before treatment

In treat group, 72 cases reieeived received gastroscope examination, 50 cases received X-Raybarium meal examination or air-barium double contrast examination, 65 cases received B type ultrasonic examination, 18 cases received CT examination.

In control group, 26 cases reieeived received gastroscope examination, 23 cases received X-Raybarium meal examination or air-barium double contrast examination, 28 cases received B type ultrasonic examination, 12 cases received CT examination.

Above results of comparability check show that there is no notable significance in the difference resulted from the comparison of sex, age, disease courses, past treatment methods, tumor type, tumor location, number and size, main clinical symptoms and signs, tongue demonstration of two groups before

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treatment, except that cancer pain extent of treat group is higher than that of control group. Suggesting that prognostic factors are uniform between two groups.

Therapeutic effects comparison

1.Total therapeutic effects comparison.

5

Table 22   Total therapeutic effects comparison

group	cases	CR(%)	PR(%)	SD(%)	PD(%)
treat group	87	1	15	63	8
		(1.1)	(17.2)	(72.4)	(9.2)
control	42	0	1	29	12
		(0.0)	(2.4)	(69.0)	(28.6)
		rank sum test	u=3.510	P=0.000	

CR, PR, SD and PD rates of treat group are 1.1%,17.2%,72.4%,9.2% respectively, total remission rate is 18.3%; CR, PR, SD and PD rates of control group are 0%,2.4%,69.0% and 28.6% respectively, total remission is 2.4% . There is notable signicance significance in the difference between two groups.

10   1 complete remission case in treat group, male, 64 years old, two years before enrollment, was diagnosed as: gastric carcinoma (adenocarcinoma), received subtotal gastrectomy. The patient feel obstruction after meal, and aggravated gradually, then visited Changzhou cancer hospital, no measurable tumor foci, pathologic diagnosis showed: cancer cells are in ulcerative necrosis tissue (maybe adenocarcinoma). According to the trail regimen, treated the patient with the invented Traditional Chinese Medicine

15   composition combined with chemotherapy. After treatment, pathologic examination showed: moderate reactive gastritis. Follow-up 7 months later and rechecked, the pathological examination showed: inflammation changes of mucosa. Therapeutic effects assessed as complete remission. Considering that the therapeutic effects assessment of this patient was not so confirm, so adopting "concessional conservation method" classified the effect as "Stable Disease", then performed clinical therapeutic effects comparison: results is shown in following table.

20

Table 23 Total therapeutic effects comparison ("concessional conservation method")

group	cases	CR(%)	PR(%)	SD(%)	PD(%)
treat group	87	0	15	64	8
		(0.0)	(17.2)	(73.6)	(9.2)
control	42	0	1	29	12

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	(0.0)	(2.4)	(69)	(28.6)

	rank sum test	u=3.445	P=0.001

Above results show that there is notable significance in the difference of total therapeutic effects resulted from comparison of two groups (u=3.445, P=0.001), after adding 1 CR case into SD case via "concessional conservation method".

2. Therapeutic effects comparison of gastric carcinoma without metastasis between two groups

Table 24 Therapeutic effects comparison of gastric carcinoma without metastasis between two groups

group	cases	CR (%)	PR (%)	SD (%)	PD (%)
treat group	62	1	10	45	6
		(1.6)	(16.1)	(72.6)	(9.7)
control	27	0	1	18	8
		(0.0)	(3.7)	(66.7)	(29.6)

	rank sum test	u=2.723	P=0.006

CR, PR, SD and PD rates of treat group are 1.6%, 16.1%, 72.6%, 9.7% respectively, total remission rate is 17.7%; CR, PR, SD and PD rates of control group are 0%, 3.7%, 66.7% and 29.6% respectively, total remission is 3.7% . There is notable significance significance in the difference between two groups.

3. Therapeutic effects comparison of gastric carcinoma with metastasis between two groups

Table 25 Therapeutic effects comparison of gastric carcinoma with metastasis between two groups

group	cases	CR(%)	PR(%)	SD(%)	PR(%)
treat group	25	0	5	18	2
		(0.0)	(20)	(72)	(8)
control	15	0	0	11	4
		(0.0)	(0.0)	(73.3)	(26.7)

	rank sum test	u=2.228	P=0.026

CR, PR, SD and PD rates of treat group are 0.0%, 20.0%, 72.0%, 8.0% respectively, total remission rate is 20.0%; CR, PR, SD and PD rates of control group are 0%, 0.0%, 73.3% and 26.7% respectively, total remission is 0.0% . There is notable significance significance in the difference between two groups.

4. Follow-up life span and survival rate comparison of two groups

Table 26 Death comparison of two groups 1.5 years after treatment

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group	cases	survival	death (cause)		
			upper gastrointestinal bleeding	failure	others
treat group	87	16	10	60	1
control	42	6	11	21	4
Combine death cases	X^2=0.34		P=0.56		

Death comparison of two groups 1.5 years after treatment, there is no notable significance in the difference.

Table 27 Life span and survival comparison of two groups 1.5 year after treatment （一）*

group	cases	complete data cases	censored	% cencored
treat group	87 .	71	16	（18.4）
control	41	35	6	（14.6）

*1 case in control group did not finish treatment course, died 1 month after treatment.

5   Table 28 Life span and survival comparison of two groups 1.5 year after treatment （二）*

group	cases	Average live time(month)	Median live time(month)	1 year survival rate	
		$\overline{x}\pm s$	$\overline{x}\pm s$	%	标准误
treat group	87	10±1	10±1	32.83	5.1
control	41	8±1	6±1	24.39	6.7
short term effect: Breslow test，statistic=4.22			P=0.040		
Long term effect: Log-rank test，statistic =1.98			P=0.1597		

* 1 case in control group did not finish treatment course, died 1 month after treatment.

Life span and survival comparison of two groups 1.5 year after treatment: survival rate of treat group and control group are 32.83%，24.39% respectively, there is notable significance in the difference of short term effect resulted from comparison of two groups; but there is no notable significance in the difference of

10   Long term effect resulted from comparison of two groups. Indicating short term effect of treat group is better than that of control group.

5. Life span and survival rate comparison of gastric carcinoma without metastasis between two groups after treatment

Table 29 Life span and survival rate comparison of gastric carcinoma without metastasis between two

15   groups after treatment （一）

83

group	cases	complete data cases	censored	% censored
treat group	62	49	13	(21)
control	27	21	6	(22.2)

Table 30 Life span and survival rate comparison of gastric carcinoma without metastasis between two groups after treatment (二)

group	cases	Average live time(month)	Median live time(month)	1 year _survival rate	
		$\overline{x} \pm s$	$\overline{x} \pm s$	%	se
treat group	62	10±1	10±1	31.27	0.061
control	27	10±1	7±2	33.33	0.091

short term effect: Breslow test, statistic=4.22=0.05	P=0.824
Long term effect: Log-rank test, statistic =1.98=0.56	P=0.454

Life span and survival rate comparison of two groups 1.5 year after treatment: survival rate of treat group and control group are 31.27%, 33.33% respectively, There is no notable significance in the difference of short term effect and long term effect resulted from comparison of two groups. Short term effect and long term effects on gastric carcinoma without metastasis, treat group are equal to control group after treatment.

6. Life span and survival rate comparison of gastric carcinoma with metastasis between two groups after treatment

Table 31 Life span and survival rate comparison of gastric carcinoma with metastasis between two groups after treatment (一) *

group	cases	complete data cases	censored	% censored
treat group	25	22	3	(12)
control	14	14	0	(0.0)

* 1 case in control group did not finish therapy course, died 1 month after treatment.

Table 32 Life span and survival rate comparison of gastric carcinoma with metastasis between two groups after treatment (二) *

group	cases	Average live time(month) $\overline{x} \pm s$	Median live time(month) $\overline{x} \pm s$	1 year survival rate %	se
treat group	25	9±1	7±2	36.0	0.096
control	14	5±1	4±1	7.14	0.069

short term effect: Breslow test， statistic =5.72 P=0.0168

Long term effect: Log-rank test， statistic =7.56 P=0.0060

* 1 case in control group did not finish therapy course, died 1 month after treatment.

Life span and survival rate comparison of two groups 1.5 year after treatment: survival rate of treat group and control group are 36.0%, 7.14% respectively. There is no notable significance in the difference of short term effect and long term effect resulted form comparison of two groups. Short term effects and long term effects on gastric carcinoma with metastasis, treat group are better than control group after treatment.

7. Tumor foci size comparison of two groups after treatment

Table 33 Tumor foci size comparison of two groups after treatment

group	cases	before treatment $\overline{x} \pm s$	after treatment $\overline{x} \pm s$	difference (after-before) $\overline{x} \pm s$	t	P
treat group	83	27.04±22.32	21.92±23.65	-5.12±8.86	5.262	0.000
control	40	26.44±48.58	26.00±46.44	-0.44±7.31	0.378	0.708
		t=0.095 P=0.925	t=0.646 P=0.519	t=2.897 P=0.004		

Tumor foci size comparison of treat group before and after treatment, there is notable significance in the difference.

Tumor foci size comparison of control group before and after treatment, there is no notable significance in the difference.

Tumor foci size difference (after-before) comparison of two groups, there is notable significance in the difference.

8. Karnofsky scores comparison of two groups after treatment

Table 34   Karnofsky scores comparison of two groups after treatment

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group	cases	before treatment $\overline{x} \pm s$	after treatment $\overline{x} \pm s$	difference (after-before) $\overline{x} \pm s$	t	P
treat group	87	66.78±8.83	81.15±8.13	14.37±10.53	12.72	0.000
control	42	69.05±9.32	74.06±11.06	5.00±13.84	2.34	0.024
		t=1.340	t=8.434	t=4.261		
		P=0.180	P=0.000	P=0.000		

Karnofsky scores comparison of treat group before and after treatment, there is notable significance in the difference .

Karnofsky scores comparison of control group before and after treatment, there is notable significance in the difference .

5 Karnofsky scores difference (after-before) comparison of two groups, there is notable significance in the difference .

9. Body weight comparison of two groups after treatment

Table 35   Body weight (Kg) comparison of two groups after treatment

group	cases	before treatment $\overline{x} \pm s$	after treatment $\overline{x} \pm s$	difference (after-before) $\overline{x} \pm s$	t	P
treat group	87	57.21±9.01	58.16±9.04	0.95±6.66	1.34	0.19
control	42	57.31±8.48	58.36±8.24	1.05±7.59	0.89	0.38
		t=0.06	t=0.119	t=0.071		
		P=0.95	P=0.906	P=0.943		

10 Body weight comparison of treat group before and after treatment, there is no notable significance in the difference.

Body weight comparison of control group before and after treatment, there is no notable significance in the difference.

15 Body weight difference (after-before) comparison of two groups, there is no notable significance in the difference.

10. Appetite comparison of two groups after treatment

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Table 36　Appetite（taels/day）　comparison of two groups after treatment

group	cases	before treatment $\overline{x} \pm s$	after treatment $\overline{x} \pm s$	difference （after-before） $\overline{x} \pm s$	t	P
treat group	87	5.47±2.01	7.93±6.36	2.46±5.79	3.97	0.000
control	42	5.81±1.29	6.62±1.81	0.81±2.23	2.35	0.024
		t=0.995	t=1.309	t=1.782		
		P=0.322	P=0.193	P=0.077		

Appetite comparison of treat group before and after treatment, there is notabe-notable significance in the difference.

Appetite comparison of control group before and after treatment, there is notabe-notable significance in
5　the difference.

Appetite difference （after-before） comparison of two groups, there is no notable significance in the difference .

11. Fatigue improvement comparison of two groups after treatment

Table 37　Fatigue improvement comparison of two groups after treatment

group	cases	aggravation	no change	Improved 1 grade	Improved 2 grades	Improved 3 grades	Improved 4 grades
treat group	74	1	7	27	32	5	2
control	33	3	5	16	6	3	0
				rank sum test	u=2.42	P=0.015	

10　* Improved 1 grade: lowered 1 grade after treatment compared with before treatment.

Improved 2 grades: lowered 2 grades after treatment compared with before treatment.

Improved 3 grades: lowered 3 grades after treatment compared with before treatment.

Improved 4 grades :lowered 4 grades after treatment compared with before treatment.

Fatigue improvement comparison of two groups after treatment, there is notabe-notable significance in
15　the difference.

12. Clinical symptoms and signs improvement comparison of two groups after treatment

Table 38 Clinical symptoms and signs improvement comparison of two groups after treatment*

symptoms	group	cases	aggrav atio	no cha nge	Improv ed 1 grade	Improved 2 grades	Improved 3 grades	Improved 4 grades	u	P

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		n								
gastric pain	treat group	77	0	9	23	32	13	0	2.43	0.02
	control	39	2	7	16	11	2	1		
anorexia	treat group	73	0	10	24	29	9	1	2.82	0.01
	control	37	3	6	19	7	1	1		
dry mouth thirst	treat group	34	0	3	24	7	0	0	0.61	0.54
	control	13	1	2	7	3	0	0		
bitter taste of mouth	treat group	34	0	5	22	5	2	0	2.47	0.01
	control	11	1	4	6	0	0	0		
spontaneous perspiration	treat group	32	0	1	17	10	4	0	1.48	0.14
	control	12	1	2	5	4	0	0		
night sweat	treat group	30	0	3	18	7	2	0	2.20	0.03
	control	9	2	2	4	1	0	0		
upset and tantrum	treat group	29	0	2	15	11	1	0	3.02	0.01
	control	10	1	3	6	0	0	0		
dizziness	treat group	22	0	2	17	2	1	0	1.39	0.17
	control	9	2	1	5	1	0	0		
cancer pain	treat group	73	1	6	29	23	12	2	2.41	0.02
	control	29	2	2	17	8	0	0		
nausea and vomit	treat group	38	0	1	22	12	2	1	2.35	0.02

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	control	16	0	5	8	2	1	0	
abdominal distension	treat group	55	1	5	29	14	6	0	1.24 0.22
	control	25	2	5	11	4	0	3	

* Improved 1 grade: lower 1 grade after treatment compared with before treatment, for example, grade □ of anorexia "without appetite, appetite decreased >1/2"; improved to grade □ of anorexia "without appetite, appetite decreased within 1/3 to 1/2", analogized sequentially.

Improventment Improvement extent comparison of gastric discomfort, anorexia, bitter mouth, night sweat, upset and tantrum, cancer pain, nausea between two groups after treatment, there is notable significance in the difference.

Improventment Improvement extent comparison of dry mouth, thirst, spontaneous perspiration, dizziness and abdominal distension between two groups after treatment, there is no notable significance in the difference

13. Main symptoms and signs disappearance rates comparison of two groups after treatment

Table 39 Main symptoms and signs disappearance rates comparison of two groups after treatment (一)

	group	gastric discomfort	anorexia	fatigue	dry mouth thirst
treat group	original cases	77	73	74	34
	disappearance cases	30	35	39	26
	disappearance rate	38.96	47.95	52.7	76.47
control	original cases	39	37	33	13
	disappearance cases	16	18	16	10
	disappearance rate	41.03	48.65	48.48	76.92
	X^2 (correction)	0.05	0.00	0.16	Fisher's exact test
	P	0.83	0.94	0.69	1.00

Table 40 Main symptoms and signs disappearance rates comparison of two groups after treatment (二)

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group		bitter mouth	spontaneous perspiration	night sweat	upset and tantrum
treat group	original cases	34	32	30	29
	disappearance cases	27	28	23	26
	disappearance rate	79.41	87.5	76.67	89.66
control	original cases	11	12	9	10
	disappearance cases	6	8	5	6
	disappearance rate	54.55	66.67	55.56	60
X^2 (correction)		Fisher's exact test	Fisher's exact test	Fisher's exact test	Fisher's exact test
P		0.24	0.18	0.23	0.057

Table 41 Main symptoms and signs disappearance rates comparison of two groups after treatment （三）

group		dizziness	Cancer pain	nausea and vomit	abdominal distension
treat group	original cases	22	73	38	55
	disappearance cases	20	44	31	35
	disappearance rate	90.91	60.27	81.58	63.64
control	original cases	9	29	16	25
	disappearance cases	6	16	8	11
	disappearance rate	66.67	55.17	50	44
X^2 (correction)		Fisher's exact test	0.22	Fisher's exact test	2.71
P		0.13	0.64	0.043	0.099

~~Disappearce~~ Disappearance rates comparison of nausea and vomit, there is notable significance in the difference.

5   ~~Disappearce~~ Disappearance rates comparison of gastric discomfort, anorexia, fatigue, dry mouth, thirst, dizziness, bitter mouth, spontaneous perspiration, night sweat, upset and tantrum, dizziness, cancer pain,

abdominal distension of two groups after treatment, there is no notable significance in the difference.

14. WBC counting comparison of two groups after treatment

Table 42 WBC counting comparison of two groups after treatment[*]

group	cases	aggravation	no change	Improved 1 grade
treat group	83	2	80	1
control	39	5	33	1
rank sum test		u=1.757	P=0.079	

* Grade WBC accurately according to "WHOgrade criterions for acute and subacute toxicity reactions of

5   the anti-cancer drugs", .see details in application example 1.

There is no notable significance in the difference of WBC counting.

15. Granulocytes counting comparison of two groups after treatment

Table 43 Granulocytes counting comparison of two groups after treatment[*]

group	cases	aggravation	no change	Improved 1 grade	Improved 2 grades	Improved 3 grades
treat group	41	1	39	1	0	0
control	22	2	18	1	0	1
rank sum test		u=0.01	P=0.99			

* Grade granulocytes accurately according to "WHO grade criterions for acute and subacute toxicity

10   reactions of the anti-cancer drugs", see details in application example 1.

There is no notable significance in the difference of Granulocytes counting.

16. Hemoglobin comparison of two groups after treatment

Table 44 Hemoglobin comparison of two groups after treatment[*]

group	cases	aggravation	no change	Improved 1 grade	Improved 2 grades	Improved 3 grades
treat group	83	8	53	15	5	2
control	40	9	25	2	3	1
rank sum test		u=1.927	P=0.054			

* Grade hemoglobin accurately according to "WHOgrade criterions for acute and subacute toxicity

15   reactions of the anti-cancer drugs"-", see details in application example 1.

There is no notable significance in difference of Hemoglobin (P=0.054 close to the clinical value),

Hemoglobin of treat group has tend to be increased , compared with control group.

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17. Platelets counting comparison of two groups after treatment

Table 45 Platelets counting comparison of two groups after treatment*

group	cases	aggravation	no change	Improved 1 grade	Improved 2 grades	Improved 3 grades
treat group	82	1	79	2	0	0
control	40	3	34	3	0	0

| | | rank sum test | u=0.223 | P=0.824 | | |

*Grade platelets accurately according to "WHOgrade criterions for acute and subacute toxicity reactions of the anti-cancer drugs", see details in application example 1.

5   There is no notable ~~significantee~~ significance in the difference of Platelets counting .

18. .Immune function comparison of two groups after treatment

Table 46 CD3 comparison of two groups before and after treatment

group	cases	before treatment $\overline{x} \pm s$	8 weeks after treatment $\overline{x} \pm s$	difference (after-before) $\overline{x} \pm s$	t	p
treat group	52	52.51±8.16	57.67±9.04	4.84±5.64	6.12	0.000
control	21	50.44±9.64	48.19±9.43	-1.25±6.19	0.808	0.432
		t=0.93	t=3.62	t=3.68		
		P=0.35	P=0.00057	P=0.00047		

CD3 comparison of two groups before treatment, there is no notable significance in the difference. .

10   CD3 comparison of two groups after treatment, there is notable significance in the difference .

CD3 difference (after-before) comparison of two groups, there is notable significance in the difference.

CD3 comparison of treat group before and after treatment, there is notable significance in the difference (t=6.12, P=0.000).

CD3 comparison of control group before and after treatment, there is no notable significance in the

15   difference. (t=0.808, P=0.432).

Table 47 CD4 comparison of two groups before and after treatment

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group	cases	before treatment $\overline{x}\pm s$	8 weeks after treatment $\overline{x}\pm s$	difference (after-before) $\overline{x}\pm s$	t	p
treat group	52	36.08±7.08	40.18±6.87	3.78±4.22	6.41	0.000
control	21	31.94±9.30	32.00±9.54	-0.63±6.44	0.39	0.703
		t=2.06	t=3.77	t=3.19		
		P=0.043	P=0.00036	P=0.0022		

CD4 comparison of two groups before treatment, there is notable significance in the difference.

CD4 comparison of two groups after treatment, there is notable significance in the difference.

CD4 after-before) of comparison of two groups, there is notable significance in the difference.

CD4 comparison of treat group before and after treatment. (t=6.41, P=0.000), there is notable significance in the difference.

CD4comparison of control group before and after treatment (t=0.39, P=0.703), there is no notable significance in the difference..

Table 48 CD8 comparison of two groups before and after treatment

group	cases	before treatment $\overline{x}\pm s$	8 weeks after treatment $\overline{x}\pm s$	difference (after-before) $\overline{x}\pm s$	t	p
treat group	51	28.67±8.54	25.69±4.35	-3.00±8.06	2.66	0.011
control	21	28.25±10.32	26.06±10.34	-1.19±3.62	1.31	0.21
		t=0.18	t=0.21	t=0.87		
		P=0.85	P=0.83	P=0.39		

CD8 comparison of two groups before treatment, there is no notable significance in the difference.

CD8 comparison of two groups after treatment, there is no notable significance in the difference.

CD8 (after-before) comparison of two groups, there is no notable significance in the difference.

CD8 of comparison of treat group before and after treatment (t=2.66, P=0.011), there is notable significance in the difference .

CD8 comparison of control group before and after treatment .(t=1.31, P=0.21), there is no notable significance in the difference.

Table 49 CD4/CD8 comparison of two groups before and after treatment

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group	cases	before treatment $\overline{x}\pm s$	8 weeks after treatment $\overline{x}\pm s$	difference (after-before) $\overline{x}\pm s$	t	p
treat group	51	1.31±0.32	1.59±0.38	0.22±0.42	6.85	0.000
control	21	1.19±0.26	1.28±0.38	0.06±0.25	0.61	0.55
		t=1.54 P=0.13	t=2.84 P=0.0059	t=1.39 P=0.17		

CD4/CD8 comparison of two groups before treatment, there is no notable significance in the difference.

CD4/CD8 comparison of two groups after treatment, there is notable significance in the difference.

CD4/CD8 （after-before） comparison of two groups, there is no notable significance in the difference.

CD4/CD8 comparison of treat group before and after treatment (t=6.85, P=0.000)., there is notable significance in the difference.

CD4/CD8 comparison of control group before and after treatment (t=0.61, P=0.55), there is no notable significance in the difference .

Table 50 NK cell comparison of two groups before and after treatment

group	cases	before treatment $\overline{x}\pm s$	8 weeks after treatment $\overline{x}\pm s$	difference (after-before) $\overline{x}\pm s$	t	p
treat group	12	16.17±1.80	18.18±3.36	2.00±1.71	4.05	0.002
control	11	16.65±6.22	15.73±3.12	-1.33±1.75	1.79	0.134
		t=0.26 P=0.80	t=1.49 P=0.16	t=3.88 P=0.0013		

NK cell comparison of two groups before treatment, there is no notable significance in the difference.

NK cell comparison of two groups after treatment, there is no notable significance in the difference.

NK cell （after-before） comparison of two groups, there is notable significance in the difference.

NK cell comparison of treat group before and after treatment (t=4.05, P=0.002), there is notable signficancesignificance in the difference.

NK cell comparison of control group before and after treatment (t=1.79, P=0.134), there is no notable significance in the difference .

19. CEA comparison of two groups before and after treatment

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Table 51 CEA comparison of two groups before and after treatment

group	cases	before treatment $\overline{x}\pm s$	8 weeks after treatment $\overline{x}\pm s$	difference (after-before) $\overline{x}\pm s$	t	p
treat group	68	18.69±20.27	17.15±18.27	-1.27±12.41	0.69	0.49
control	31	17.58±19.79	17.04±20.17	0.37±4.81	0.40	0.69
		t=0.25	t=0.03	t=0.37		
		P=0.79	P=0.98	P=0.72		

CEA comparison of two groups before treatment, there is no notable significance in the difference.

CEA comparison of two groups after treatment, there is no notable significance in the difference.

CEA (after-before) comparison of two groups, there is no notable significance in the difference.

CEA comparison of treat group before and after treatment (t=0.69, P=0.49), there is no notable significance in the difference.

CEA comparison of control group before and after treatment (t=0.40, P=0.69), there is no notable significance in the difference.

20. Bleeding time and coagulation time comparison of two groups before and after treatment

Table 52 Bleeding time (second) comparison of two groups before and after treatment

group	cases	before treatment $\overline{x}\pm s$	8 weeks after treatment $\overline{x}\pm s$	difference (after-before) $\overline{x}\pm s$	t	p
treat group	40	115.08±22.35	117.76±20.19	2.68±18.49	0.88	0.38
control	20	107.25±29.36	109.17±35.74	3.33±22.29	0.63	0.53
		t=1.15	t=1.14	t=0.12		
		P=0.26	P=0.26	P=0.91		

Bleeding time comparison of two groups before treatment, there is no notable significance in the difference .

Bleeding time comparison of two groups after treatment, there is no notable significance in the difference

Bleeding time (after-before) comparison of two groups, there is no notable significance in the difference

Bleeding time comparison of treat group before and after treatment (t=0.88, P=0.38), there is no notable

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significance in the difference.

Bleeding time comparison of control group before and after treatment (t=0.63, P=0.53), there is no notable significance in the difference.

5   Table 53 Coagulation time (second) comparison of two groups before and after treatment

group	cases	before treatment $\overline{x} \pm s$	8 weeks after treatment $\overline{x} \pm s$	difference (after-before) $\overline{x} \pm s$	t	p
treat group	40	156.33±28.09	154.51±31.91	-0.70±15.69	0.27	0.79
control	20	158.50±40.91	154.72±42.51	1.94±16.64	0.49	0.63
		t=0.24	t=0.02	t=0.58		
		P=0.81	P=0.98	P=0.57		

Coagulation time comparison of two groups before treatment, there is no notable significance in the difference .

Coagulation time comparison of two groups after treatment, there is no notable significance in the difference

10   Coagulation time difference (after-before) comparison of two groups, there is no notable significance in the difference

Coagulation time comparison of treat group before and after treatment (t=0.27, P=0.79), there is no notable significance in the difference.

Coagulation time comparison of control group before and after treatment (t=0.49, P=0.63), there is no

15   notable significance in the difference.

四. Safety assessment

All safety indexes are normal before treatment, the safety assessment results of the abnormal after treatment are recorded in following table:

doubtful adverse reaction	treat group		control group		RR	P
	positive cases/total cases	incidence rate	positive cases/total cases	incidence rate		
Hemoglobin reduction	3/48	6.3%	4/20	20.0%	0.31	0.182
WBC reduction	2/80	2.5%	4/35	11.4%	0.22	0.069

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Granulocyte reduction	1/42	0.5%	1/26	3.8%	0.62	1.00
Platelet reduction	1/81	1.2%	3/38	7.9%	0.16	0.095
Bilirubin increase	5/72	6.9%	4/35	11.4%	0.61	0.470
AKP rising	5/56	8.9%	5/36	13.9%	0.64	0.505
GPT rising	2/79	2.5%	1/37	2.7%	0.94	1.00
BUN rising	2/81	2.5%	5/38	13.2%	0.19	0.033
serum creatinine rising	0/85	0.0%	2/42	4.8%		0.108
Abnormal urine protein	1/85	1.2%	1/39	2.6%	0.46	0.532
~~Abnormal~~ Abnormal urine WBC	0/86	0.0%	1/42	2.4%		0.328
~~Abnormal~~ Abnormal urine RBC	0/85	0.0%	1/41	2.4%		0.325
mucous stool	0/79	0.0%	3/41	7.3%		0.038
faeces RBC abnormality	2/79	2.5%	3/41	7.3%	0.35	0.337
faeces WBC abnormality	3/86	3.5%	3/42	7.1%	0.49	0.393
fecal occult blood	0/51	0.0%	1/22	4.5%		0.301

Safety indexes assessment results of two groups after treatment demonstrate that incidence rates of BUN rising, mucous stool of treat group are lower than those of control group (P<0.05); The statistical analysis results of incidence rate demonstrate that there is no notable significance in the difference of other items of two groups. See details in above table.

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Adverse event observations

Table 54 Results of adverse event observations of two groups after treatment

doubtful adverse reaction	treat group (n=87)		control group (n=42)		RR	P
	positive cases[*]	incidence rate	Positive cases[*]	incidence rate		

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alopecie	9	10.3%	4	9.5%	1.09	1.000
oral cavity ulcer	1	1.1%	1	2.4%	0.48	0.547
cutaneous reaction	1	1.1%	0	0%		1.000
choking and short of breath	4	4.6%	2	4.8%	0.97	1.000
jaundice	1	1.1%	4	9.5%	0.12	0.039
non cancer pain	4	4.6%	6	14.3%	0.32	0.077
hypersensitiveness	3	3.4%	2	4.8%	0.72	0.660
hemafecia	2	2.3%	3	7.1%	0.32	0.329
constipation	1	1.1%	2	4.8%	0.24	0.247
diarrhea	5	5.7%	4	9.5%	0.60	0.472
haematemesis	0	0%	0	0%		

*positive cases: if one patient had one symptom, recorded as one case, if one patient had two symptoms, recorded as two cases.

During the courses of treatment, some patients in both groups had adverse reaction including baldness, oral ulcer. The incidence rates of symptoms and statistical comparison results of two groups demonstrate

5   that jaundice incidence rate of treat group is lower than that of control groups, and there is no notable significance in difference of other adverse reaction of two groups, see details in above table.

There are 25 cases in treat group who has at least one doubtful adverse reaction, and total incidence of doubtful adverse reaction is 28.7% (25/87); there are 17 cases in control group who had at least one doubtful adverse reaction, and total incidence of doubtful adverse reaction is 40.5% (17/42) , there is no notable

10   significance in difference of adverse reaction of two groups (RR=0.71, P=0.182).

Conclusions

129 eligible tested object, of which, 87 cases in treat group, 42 cases in control group; all are diagnosed as gastric carcinoma by westenwestern medicine and as symptom of stagnation of poison by Traditional

15   Chinese Medicine, 15 outpatient cases, 114 inpatient cases.

Results of comparability check show that there is no notable significance in differences of sex, age, disease courses ,past treatment methods, tumor type, tumor location, number and size, main clinical symptoms and signs, tongue demonstration of two groups before treatment , except that cancer pain of treat group is more than that of control group. It suggests that prognostic main factors are uniform between

20   two groups with comparability.

Results of total clinical therapeutic effects demonstrate:

CR, PR, SD and PD rates of treat group are 1.1%, 17.2%, 72.4%, 9.2% respectively, total remission rate

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is 18.3%; CR, PR, SD and PD rates of control group are 0%, 2.4%, 69.0% and 28.6% respectively, total remission is 2.4%. There are notable significance in difference of two groups.

Clinical therapeutic effects results on gastric carcinoma without metastasis show that CR, PR, SD and PD rates of treat group are 1.6%, 16.1%, 72.6%, 9.7% respectively, total remission rate is 17.7%; CR, PR, SD and PD rates of control group are 0%, 3.7%, 66.7% and 29.6% respectively, total remission is 3.7%. There are notable significance in difference of two groups.

Clinical therapeutic effects results on gastric carcinoma with metastasis show that CR, PR, SD and PD rates of treat group are 0.0%, 20.0%, 72.0%, 8.0% respectively, total remission rate is 20.0%; CR, PR, SD and PD rates of control group are 0%, 0.0%, 73.3% and 26.7% respectively, total remission is 0.0%. There are notable significance in difference of two groups.

Therapeutic effect of 1 case in treat group shown as "complete remission", Considering that the therapeutic effects assessment of this patient was not confirmed, so we adopted "concessional conservation method" and classified the effect as "Stable Disease", then performed clinical therapeutic effects comparison. There is notable significance in difference of the two groups (u=3.445, P=0.001), and results are shown in table 23.

Above results indicate that the invented Traditional Chinese Medicine composition, combined with chemotherapy on treatment of gastric carcinoma (belonging to the sympton symptom of stagnation of poison), has better clinical therapeutic effects, exerting certain synergistic functions and adjunctive therapeutic functions.

Results of life span and survival rate assessment:

1.5 year follow-up after treatment, survival rate of treat group and control group are 32.83%, 24.39% respectively, there is notable significance in difference of short term effect of two groups; there is no notable significance in difference of: long term effect of two groups

For gastric carcinoma without metastasis patients, 1.5 year: follow-up after treatment, survival rate of treat group and control group are 31.27%, 33.33% respectively, there is no notable significance in difference of short term effect of two groups; there is no notable significance in difference of: long term effect of two groups .

For gastric carcinoma metastasis patients, 1.5 year follow-up after treatment, survival rate of treat group and control group are 36.0%, 7.14% respectively, there is notable significance in difference of short term effect of two groups; there is notable significance in difference of long term effect of two groups .

Indicating that the invented Traditional Chinese Medicine composition, serving as adjunctive therapy on chemotherapy of gastric carcinoma (considered as symptom of stagnation of poison by Traditional Chinese Medicine) short term effect is better than sole chemotherapy, long term effect is equal to sole

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chemotherapy (for gastric carcinoma patients with metastasis, short term effect and long term effect all are better than sole chemotherapy).

Results of solid ~~temor~~ tumor foci size assessment show:

5   There is notable significance in difference of tumor foci size difference（after-before）of two groups, minimized extent of the tumor foci size of treat group is greater than that of control group. There is notable significance in difference of tumor foci size of treat group before and after treatment, tumor minimized obviously after treatment compared with before treatment~~;~~. There is no notable significance in difference of tumor foci size of control group before and after treatment. Suggesting that the invented

10   Traditional Chinese Medicine composition, serving as adjunctive therapy on chemotherapy of gastric carcinoma (considered as symptom of stagnation of ~~posison~~ poison by Traditional Chinese Medicine), can minimize tumor foci obviously, which outweighs therapeutic effects of sole chemotherapy.

Results of main symptoms improvement show:

15   Karnofsky score of both treat group and control group increased obviously after treatment compared with that of before treatment, and the Karnofsky score increased extent of treat group is greater than control group; Fatigue of patients in both groups are improved obviously after treatment, fatigue improvement extent of treat group is greater than that of control group.

20   Appetite of patients in both groups increased obviously, symptoms including gastric discomfort, anorexia, dry mouth, thirst, bitter mouth, spontaneous perspiration, night sweat, upset, tantrum, cancer pain, nausea and vomit, abdominal distension, are all improved or have high disappearance rates, for improvement extent of gastric discomfort, anorexia, bitter mouth, night sweat, upset, tantrum, cancer pain, nausea and vomit, treat group is higher than that of control group. There is no notable significance in

25   difference of improvement and disappearance rates of other symptoms between two groups .

Above results indicate that the invented Traditional Chinese Medicine composition, serving as adjunctive therapy on chemotherapy of gastric carcinoma, can ameliorate patients survival qualities, improve clinical symptoms and has better adjunctive ~~therapeutical~~ therapeutic effects.

30   Laboratory examination results demonstrate:

WBC, RBC, platelet of two groups did not ~~ineease~~ increase obviously after treatment compared with before treatment, hemoglobin of two groups increased obviously after treatment, and there is notable significance in difference of hemoglobin comparison of two groups after treatment (P=0.054), Hemoglobin of treat group has   tend to be increased, compared with control group.

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CD3, CD4 , CD4/CD8 and NK cells of treat group increased obviously after treatment compared with those of before treatment($P<0.05$), furthermore, the CD3, CD4 and NK cell difference(after-before)of treat group are higher than those of control group($P<0.05$), while changes of CD3、CD4 , CD4/CD8 and NK cells of control group are not so obvious.

5   Above results indicate that the invented Traditional Chinese Medicine composition, serving as adjunctive therapy on chemotherapy of gastric carcinoma, has certain functions of stimulating immune responses, and can assist intervention chemotherapy to inhibit cancer cells.

Results of safety assessment show:

After treatment, some patients in two groups had hemoglobin reduction, WBC reduction, bilirubin rising,
10   AKP rising, ALT rising, BUN rising (see details in "safety assessment"), incidence rates of BUN rising , mucous stool of treat group are lower than those of control group ($P<0.05$), there is notable   significance in difference of other items of two groups .Considering that treat group received the invented Traditional Chinese Medicine composition based on chemotherapy, while control group received sole chemotherapy, it has already reported that the above side effects could also be seen during chemotherapy, so above safety
15   assessment has not determined yet that the invented Traditional Chinese Medicine composition can damage hematopoietic systems and heart, liver functions. We should perform aggregate analysis using safety assessment data of sole treatment of primary hepatic carcinoma and gastric carcinoma with the invented Traditional Chinese Medicine composition (data23-1).

Results of adverse event demonstrate:

20   During the courses of treatment, some patients in two groups had adverse reactions including alopecie, dental ulcer, scytitis, choking and short of breath, jaundice, hypersensitivity etc(see details in table 54), jaundice incidence rate of treat group is lower than that of control groups, there is no notable significance in differences of other adverse events of two groups There are 25 cases in treat group who had at least one doubtful adverse reaction, total incidence of doubtful adverse reactions is 28.7% (25/87), there are 17 cases
25   in control group who had at least one doubtful adverse reaction, total incidence of doubtful adverse reactions is 40.5% (17/42). There is no notable significance in difference of two groups (RR=0.71, P=0.182).

In summary, results of this randomized controlled trial demonstrate that the invented Traditional Chinese Medicine composition, combined with chemotherapy on treatment of gastric carcinoma, has better
30   clinical therapeutic effects, can exert synergistic functions, can ameliorate patients survival qualities, improve clinical symptoms of patients and enhance cellular immune function of patients, it can be used as adjunctive therapy on chemotherapy of gastric carcinoma patients (considered as sympton symptom of stagnation of poison by Traditional Chinese Medicine) and clinical application is quite safe.

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